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PERFRINGENS ANTITOXIN AND EXPERIMENTAL INTESTINAL OBSTRUCTION *

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Though there had accumulated an extensive literature on the subject of anaerobes, and though much had been learned about gas gangrene from a surgical point of view, not only before but during the World War, it was only in 1918 that a polyvalent antitoxic serum [1] was elaborated both for preventive and for curative use. In 1917, Bull and Pritchett [2] proved beyond all doubt the practical value of *B. welchii* antitoxin, and thus led the way for the production of the polyvalent serum that contains not only the antitoxin *to B. welchii*, but to *Vibrion septique* and *B. oedematiens* as well. It has been chiefly since the war, therefore, in the rare occasions of civil practice, that the more efficient serum has been employed. It would seem from a fair number of cases reported that the efficacy of antigas gangrene serum was comparable to that of the antitoxin of *B. diphtheriae*.

While it is clear that there would be a specific indication for the employment of an antigas gangrene serum in the case of an obvious anaerobic infection of a wound, there are many other conditions in which it has been employed when the indications are not so obviously defined. In the main, these consist of the following: intestinal obstruction, gangrenous appendicitis, general peritonitis, pulmonary gangrene, etc. A polyvalent serum has been used in France for some time as a therapeutic agent in cases of gangrenous appendicitis, and the results appear to indicate a definite reduction of mortality. The theoretical basis for its use was founded on the finding of *B. welchii* in many cases of acutely diseased appendixes. An examination of the American literature reveals that the use of the same type of serum has been followed by favorable results in a corresponding variety of cases.

Prompted probably in large measure by these successes and based on both clinical and experimental investigation, there has recently

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1. Anaerobic Infections of Wounds, Medical Research Committee Reports, 1919.

2. Bull and Pritchett: J. Exper. Med. **26**:119, 1917. (Bull: J. Exper. Med. **26**:603, 1917.)

appeared, in a convincing article by Williams, a British surgeon,[3] a new hypothesis that the toxemia in cases of intestinal obstruction, whether organic or secondary to peritonitis, resulted, in part at least, from the absorption of the toxin of *B. welchii*, due to the proliferation of this anaerobe in the stagnant contents of the small intestine. In support of this hypothesis, evidence is given of the proliferation of *B. welchii* in the small intestine in cases of intestinal obstruction and peritonitis in human subjects and in these diseases experimentally produced. Evidence of the presence of *B. welchii* toxin and its absorption is also given, while the beneficial results from the therapeutic test of the hypothesis, by giving *B. welchii* antitoxin in a series of cases of appendicular appendicitis and acute intestinal obstruction, are also reported.

The employment of such an antitoxic serum in the grave conditions of acute intestinal obstruction and general peritonitis with what appears to be a decided fall in the mortality, is surely a great achievement. In an effort to substantiate the foregoing hypothesis on an experimental basis alone, we have undertaken certain investigations, the outcome of which has convinced us that much has yet to be done to explain the toxemia of the diseases just mentioned.

EXPERIMENTAL STUDIES

I. *B. Perfringens Antitoxin in Dogs with Simple Intestinal Obstruction.*—In forty-two small dogs, a simple intestinal obstruction was induced high up in the small bowel. Each animal was given ¼ grain (0.016 Gm.) of morphine and ether anesthesia before operation. In each instance the bowel was doubly clamped about 6 inches (15.24 cm.) below the duodenaljejunal junction, cut across, the ends turned in by the Parker-Kerr method and reinforced by a double row of mattress sutures.

Eleven of these animals were used as controls. Nine were given horse serum daily. Ten were given injections of diphtheria antitoxin, while the remaining twelve were given daily subcutaneous injections of *B. perfringens* antitoxin. The first group or control animals was not given any treatment. All were allowed to drink as much water as they chose. They were offered food, but rarely ate.

The second series was given normal horse serum, 5 cc., each day, subcutaneously. The serum used was supplied by the Parke Davis Company and contained a preservative.

The third group was given 5 cc. of diphtheria antitoxin that contained 650 units per cubic centimeter. The injections were also made daily and subcutaneously.

The final series of dogs was given daily injections of 5 cc. of perfringens antitoxin, which was procured from the Mulford Company of Philadelphia, and was standardized so that 1 cc. of the serum would neutralize 1,000 minimal lethal dose of perfringens toxin.

The duration of life of each of these animals is shown in table 1. The injections of serum were begun on the day after operation. It will be seen that three animals in each series, except that given the horse serum, were found at

3. Williams: Brit. J. Surg. **14**:295, 1926.

autopsy to have some degree of peritonitis that must surely have shortened their lives. The peritoneum in the other thirty-three dogs was normal grossly. The average duration of life of those dogs without peritonitis in series D, it must be admitted, was slightly greater than in the others. This, however, is not the case when the animals with peritonitis are included. Finally, it is obvious that no material difference can be emphasized between any of the groups, and the dog that lived the longest, peculiarly enough, received diphtheria antitoxin.

II. *B. Perfringens Antitoxin in Dogs with Isolated Intestinal Loop.*—In five instances an isolated intestinal loop was made that contained a portion of the duodenum and jejunum, while the intestinal tract was reestablished by a lateral anastomosis. As a general rule such animals die from two to five days after the operation. At autopsy, there is found either a perforation of the loop, which is by far the more common occurrence, or a moderately distended one, unruptured. The death of an animal some days after such an operation and the absence of a perforation in the loop is, so far as we are aware, the best proof extant that a toxic substance is absorbed from the loop and is the lethal agent. In any experiment with an isolated loop, the contents of the loop will be found, after twenty-

TABLE 1.—*Duration of Life in Each Group of Animals*

Cause of Death	Number	Duration of Life, Days	Average Duration of Life of Toxemic Animals, Days	Average Duration of Life of Whole Group, Days
Series A. Controls—11 Animals				
Toxemia	8	2 3 5 7 7 12 12 16	8.0	6.8
Toxemia and general peritonitis	1	4		
Toxemia and local peritonitis	2	4 3		
Series B. Horse Serum—9 Animals				
Toxemia	9	3 3 4 5 6 10 11 14 15	8.8	8.8
Series C. Diphtheria Antitoxin—10 Animals				
Toxemia	7	2 2 6 7 10 15 24	9.4	8.9
Toxemia and general peritonitis	2	7 12		
Toxemia and local peritonitis	1	4		
Series D. Perfringens Antitoxin—12 Animals				
Toxemia	9	3 5 6 8 10 11 11 14 21	9.8	8.0
Toxemia and general peritonitis	1	2		
Toxemia and local peritonitis	2	2 4		

four hours, to possess a toxin which it is supposed is the lethal agent, not only in these experiments but also in simple obstruction.

Each of the five animals so prepared was given 5 cc. of perfringens antitoxin subcutaneously on successive days, beginning twenty-four hours after operation. The duration of life of each animal was two, five, five, eight and thirteen days, respectively, with an average of 6.6 days. At autopsy each dog was found to have general peritonitis resulting from a rupture of the loop.

III. *Isolated Loop Toxin and B. Perfringens Antitoxin Mixed and Injected Intravenously.*—Loop toxin was procured by the following procedure: A duodenojejunal loop was made in the usual manner, and after forty-eight hours the animal was killed. The isolated loop was removed, incised and its contents added to 40 cc. of physiologic sodium chloride solution in which the loop was thoroughly washed. The material was then filtered through about six layers of gauze to remove any gross matter. The whole process would consume not more than from fifteen to twenty minutes when it was used for injection. To three control dogs, 2.5, 5 and 8 cc. were given intravenously. The same amounts were injected into three others, though to each there had been added an equal quantity of perfringens antitoxin and the mixture allowed to stand a few minutes. That is,

in the second group, one animal was given intravenously 2.5 cc. of the toxic fluid and 2.5 cc. of antitoxin; the second received 5 cc. of toxic fluid and 5 cc. antitoxin, and the third 8 cc. of each. All the animals became profoundly sick. They vomited, passed urine and feces. They behaved in the manner already described by many observers. As will be seen by table 2, only two animals lived, one that was much larger than the rest. All three animals that were given antitoxin with the toxic fluid succumbed in eight hours. The autopsies revealed the same pathologic condition as has been described elsewhere by other investigators who injected loop toxin into animals.

IV. *Isolated Loop Toxin Injected Intravenously into Dogs Immunized to Perfringens Toxin.*—Seven dogs were successfully immunized to perfringens toxin. This was accomplished in the same manner as has been done in rabbits and horses. Perfringens toxin was procured from the Mulford Company, Philadelphia, in two lots, one that contained 2 minimal lethal dose per cubic centimeter, and a second that contained 2.5 minimal lethal dose per cubic centimeter. An initial dose of 2 cc. of toxin was given subcutaneously. One week later 4 cc. were given, then 5 cc. the third week, and this repeated till the fifth or sixth week, when the dogs were found to have a moderate degree of immunity. Following the first subcutaneous injection, an area of induration and tenderness would appear at the

TABLE 2.—*Data on Animals Given Isolated Loop Toxin and B. Perfringens*

Dog	Approximate Weight, Pounds	Loop Toxin, Cc.	Perfringens Antitoxin, Cc.	Immediate Result	Final Result
1. M 31.....	15 (6.8 Kg.)	2.5	...	Moderate shock	Lived
2. D. R.	25 (11.3 Kg.)	5.0	...	Moderate shock	Lived
3. P. D.	10 (4.5 Kg.)	8.0	...	Extreme shock	Dead in 5 minutes
4, M 9.....	15	2.5	2.5	Moderate shock	Dead in 8 hours
5. M 29.....	15	5.0	5.0	Extreme shock	Dead in 8 hours
6. M 30.....	10	8.0	8.0	Extreme shock	Dead in 8 hours

site and persist for a few days. In one or two instances no such areas formed, but these animals did not possess a natural immunity to perfringens toxin. The second, third and fourth injections brought forth smaller areas of reaction, so that when a definite immunity could be proved by a test of the dog's serum, little response was noted at the site of injection of the toxin.

At varying periods the dogs were bled and their serum employed to protect pigeons against lethal doses of the perfringens toxin. No attempt was made to procure a maximum degree of immunity in these animals, and for the most part a serum the strength of which was such that 1 cc. would protect against 25 minimal lethal dose was considered satisfactory. In fact, the actual strength of the serum of each animal was not determined, but a minimum of 0.1 cc. serum to neutralize 1 cc. of toxin was set as essential. The strength of each serum will be seen in table 3. In two dogs, it was below this level.

These animals with an active immunity to perfringens toxin were given injections of isolated loop toxin. The toxic fluid was prepared in the same way as that already recorded and each animal was given what was considered to be a minimum lethal dose for a normal dog of the same weight. In series A, table 3, three animals died following an injection of 5 cc. toxic fluid which was not lethal to the normal control dog. The fourth dog died almost immediately when it was given, some days later, 7 cc. of toxic fluid, which was also fatal to a control dog. In series B, table 3, 7.5 cc. is found to be a fatal dose for both immunized animals and the normal control. The three animals were dead in from three to four hours and showed the usual pathologic condition.

The seventh dog's serum did not possess as great powers of neutralization, and 1 cc. of serum would only protect against 2.5 minimal lethal dose. This animal died three hours after an injection of 10 cc. of toxic loop fluid. A similar quantity was fatal in a control animal in eight hours.

These experiments clearly show that dogs that are immunized to the toxin of *B. perfringens* do not possess any greater power of resistance than do normal animals to a minimal lethal dose of loop toxin.

V. *Isolated Loop Toxin Injected Intramuscularly into Pigeons Protected with Dog's Immune Serum.*—The experiments reported here were done in two series and the data condensed in tables 4 and 5. They are comparable to the procedure already reported in which toxic loop fluid was mixed with commercial antitoxin and injected into dogs intravenously.

The loop toxin was prepared in the manner already described. In the first series the serum was obtained from two dogs, M 81 and M 82. One tenth of a cubic centimeter of the serum from these animals was known to protect pigeons against 2.5 minimal lethal dose of *B. perfringens* toxin. One cubic centimeter of

TABLE 3.—*Data on Immunized and Control Animals Given Toxic Loop Fluid*

Animal Injected	Quantity of Dog's Serum Necessary to Neutralize 2.5 Minimal Lethal Dose of Perfringens Toxin, Cc.	Toxic Loop Fluid		Result
		Amount, Cc.	From Dog	
		Series A		
1. O 87	Control	5.0	M 94	Sick; lived
2. M 87	0.1	5.0	M 94	Dead in 12 hours
3. M 78	0.1	5.0	M 94	Dead in 4 days
4. M 86	0.5	5.0	M 94	Dead in 5 days
5. M 85	0.1	5.0	M 94	Sick; lived
		Series B		
6. M 91a	Control	7.5	M 91	Dead in 3 hours
7. M 81	0.1	7.5	M 91	Dead in 4 hours
8. M 82	0.1	7.5	M 91	Dead in 4 hours

the serum of these dogs, that is, sufficient antitoxin to protect against 25 minimal lethal dose of toxin, was injected into the pectoral muscle of each of six pigeons after it had been allowed to stand for some minutes mixed with 1 cc. of toxic loop fluid. Each of these pigeons was found dead in eighteen hours, as were two others that received 1 cc. of loop toxin alone.

In the second series, the serum of three other dogs was employed. The strength of the serum of each animal was the same as that in the first series. One cubic centimeter of this was given to each of three pigeons that also received 0.25 cc. of toxic loop fluid. Three other pigeons received 0.5 cc. of loop toxin and 1 cc. of serum. Two pigeons received respectively 0.5 cc. and 0.25 cc. of loop toxin alone. Of the eight pigeons that were given injections of loop toxin alone, all but one were dead in thirty-one hours. A control pigeon that received 1 cc. of dog's immune serum remained well. Two other pigeons that received 1 cc. of perfringens toxin were dead in twelve hours.

Something may be said about the area in the pectoral muscle into which was injected perfringens toxin and toxic loop fluid. When perfringens toxin was used, there was a distinct edema of the breast and the subcutaneous tissues appeared gelatinous and hemorrhagic. When loop toxin was injected, there was less local edema and no hemorrhagic exudate in the subcutaneous tissues.

VI. *The Degree of Anemia that Follows the Injection of Loop Toxin.*—Intravenous injections of sublethal doses of the toxic fluid obtained from isolated loops were given to ten dogs. The degree of anemia produced after the injection is best shown in table 6. In four dogs, sublethal doses of perfringens toxin were given intravenously. The degree of anemia in these cases is shown in table 7. In the former group it must be confessed that, though the dosage employed is said to be sublethal, a few dogs, not included in the table, died before the hemoglobin was determined after the injection. Again, it must be borne in mind that the material thus injected, containing toxin as it does, is also grossly infected, so that a considerable degree of error is introduced into these determinations. More or less on this account the method of determining the hemoglobin has been by the rough method of the Talquist scale.

TABLE 4.—*Data on Pigeons Protected with Dog's Immune Serum and Given Loop Toxin*

Number	Pigeon's Marking	Amount of Loop Toxin, Cc.	Immune Serum		Result
			Amount, Cc.	From Dog	
1	1 F L W	1.0	1.0 (saline)	.....	Dead in 6 hours
2	4 F R W	1.0	1.0 (saline)	.....	Dead in 18 hours
3	3 F R W	1.0	1.0	M 81	Found dead, 18 hours
4	B H	1.0	1.0	M 81	Found dead, 18 hours
5	2 T L F	1.0	1.0	M 81	Found dead, 18 hours
6	2 F L W	1.0	1.0	M 82	Found dead, 18 hours
7	None	1.0	1.0	M 82	Found dead, 18 hours
8	B W E	1.0	1.0	M 82	Found dead, 18 hours

TABLE 5.—*Data on Pigeons Protected with Dog's Immune Serum and Given Loop Toxin and Perfringens Toxin*

Number	Pigeon's Marking	Amount Loop Toxin, Cc.	Amount Perfringens Toxin, Cc.	Immune Serum		Result
				Amount, Cc.	From Dog	
1	1 F E W	0.25	...	1.0	M 78	Dead; 20 hours
2	2 F R W and 1 F L W	0.25	...	1.0	M 85	Dead; 12 hours
3	1 F R W and 2 F	0.25	...	1.0	M 78	Lived
4	2 F E W	0.50	...	1.0	M 87	Dead; 12 hours
5	3 F L W	0.50	...	1.0	M 86	Dead; 30 hours
6	2 F R W	0.50	...	1.0	M 78	Dead; 12 hours
7	4 F L W	0.50	...	...	.....	Dead; 44 hours
8	2 F L W	0.25	...	...	.....	Dead; 30 hours
9	1 F L W	....	1.0	...	.....	Dead; 12 hours
10	1 F R W	....	1.0	...	.....	Dead; 12 hours
11	4 F R W	....	...	1.0	M 78	Lived

In the case of the *B. perfringens* toxin, the dose was well below the lethal amount. Fifteen cubic centimeters were injected into each animal although the fatal dose is somewhere about 30 for a small dog, while those used in the experiments were rather large animals. Hence we feel that the percentage fall of hemoglobin, though greater than in the series in which loop toxin was used, is not as great as it probably would have been had a larger dose been given or a lethal one injected.

However, though the control series in this group of cases is small and the degree of anemia produced by the *B. perfringens* toxin not great, there is a definite difference to be noted between the two groups. In the series in which *B. perfringens* toxin was used, there was an average fall of hemoglobin of 25.4 per cent. In the series in which loop toxin was injected the average fall of hemoglobin was only 5.6 per cent. Admitting that the methods employed allow for a certain degree

of error and that the experiment in itself was rather crude, it would still appear that the hemolytic power of the perfringens toxin was definitely greater than that of the toxic substance or substances contained in an isolated intestinal loop.

COMMENT

A further word or two must be said by way of explanation in some of the experiments described. In section I, it is observed that in one group of dogs with intestinal obstruction, series B, horse serum was injected into the animals. As perfringens antitoxin is made up largely of horse serum, it was necessary to determine the effect, if any, of this

TABLE 6.—*Degree of Anemia Produced in Ten Dogs Following Injections of Loop Toxin*

Animal	Loop Toxin, Cc.	Hemoglobin per Cent Before Injection	Hemoglobin per Cent After Injection					
			20 Hours	22 Hours	24 Hours	45 Hours	48 Hours	72 Hours
1. O 87	1.5	85	80	..	..	..	..	..
2. B S	1.0	100	..	..	..	100	..	..
3. P D	0.5	70	..	..	..	70	..	..
4. O 90	1.0	90	..	..	..	90	..	..
5. O 88	1.0	90	..	..	..	90	..	..
6. O 89	1.0	85	..	..	..	85	..	..
7. O 88	1.0	80	..	75	..	Dead	..	..
8. M 107	1.0	85	..	..	80	..	80	80
9. M 108	1.0	90	..	..	95	..	80	85
10. M 109	1.0	90	..	..	85	..	70	85

TABLE 7.—*Degree of Anemia Produced in Four Dogs Following Injections of Perfringens Toxin*

Animal	Perfringens Toxin, Cc.	Hemoglobin per Cent Before Injection	Hemoglobin per Cent After Injection		
			20 Hours	42 Hours	96 Hours
1. M 98	15*	100	95	80	85
2. M 99	15*	100	100	85	80
3. M 100	15†	110	100	75	75
4. M 101	15†	100	85	75	75

* Each cubic centimeter contains 2 minimal lethal doses for 350 Gm. pigeon.
† Each cubic centimeter contains 2.5 minimal lethal doses for 350 Gm. pigeon.

foreign serum on the animal with intestinal obstruction. So, too, series C, the animals that received diphtheria antitoxin, offered a further opportunity to observe the effect of horse serum, but also of a serum rich in antibodies, though not of a type particularly related to the condition under investigation.

The reason for employing 5 cc. of perfringens antitoxin as a dose in the animals of series D with intestinal obstruction was because that quantity was estimated to give the animal a few more units per kilogram than that suggested by Williams to be given to human beings. The dogs used in these experiments were practically all about the same size and would weigh about 5 Kg.

It must be admitted, of course, that such an experiment as described in the first section is a rather crucial test, and the antitoxic serum is

called on to be of use in a condition which in the end must result in death if not relieved. The serum employed, too, contains antitoxin to *B. perfringens* alone. However, even though cognizance is taken of these two facts, it is to be doubted if the serum given these animals was of any real value in serving to prolong their lives.

In the neutralization experiments in which loop toxin is mixed with *B. perfringens* (Mulford) antitoxin and injected intravenously into dogs, the results are comparable to those in which loop toxin was mixed with immunized dog's serum and injected intramuscularly into pigeons. To each of these groups of experiments, as well as to any that deal with the isolated loop toxin, there is the following objection: Absolute proof is wanting that the toxin contained in isolated loops is the same as that absorbed from the intestine in cases of intestinal obstruction. However, should it be the toxin of *B. welchii* that is the lethal agent, then the dogs and pigeons just mentioned should have been saved. It is our feeling that one or many extremely toxic products are contained in these loops, and that they for the most part are little changed by attempted neutralization with *B. welchii* antitoxin.

Still another point to be made concerning the toxic loop fluid that we have employed is brought out in section IV and probably again in section VI. Two dogs, M 78 and M 86, that were immunized to *B. perfringens* toxin, received intravenous injections of loop toxin that were just less than the lethal amount. Though these animals were extremely sick following the injection and died in four and five days, respectively, the cause of death was not only due to the injected toxin, but also to a moderate degree of pneumonia that followed from the introduction of infected matter into the blood stream. However, had a slightly larger dose been employed this complication would not have been encountered, as is shown in series B of the same group of experiments. In section VI, too, is found another late result of injecting this grossly infected material. Dog M 109 was given an injection of 1 cc. of loop toxin intravenously. The hemoglobin of this animal fell more than did the others in this series. Nine days after this injection the animal, which had not appeared well, died rather suddenly. At autopsy, there was found an acute and extensive inflammation of the gallbladder with perforation, and general peritonitis.

A word or two may also be said about the response of the animal and the autopsy observations following lethal injections of loop toxin and perfringens toxin. To each of two dogs, weighing nearly 5 pounds (2.3 Kg.), there was given 30 cc. of *B. perfringens* toxin intravenously. One was dead in four hours, the other found dead in eighteen hours. In each case following the injection there was moderate ataxia, apparent weakness of the hind limbs, a dazed appearance and slow movements; finally the animal crept away to a corner to remain inactive. The

autopsy, besides degenerative changes, showed definite evidence of hemolysis, and bloody fluid was found in the cavities of the chest and the abdomen. There was no unusual congestion of the duodenum.

The description of a dog into which loop toxin is injected has been made on many occasions, but by way of contrast must be repeated here. The animal apparently soon experiences pain. He yelps and begins to run about the room aimlessly and confused. He falls shortly to the floor, where he passes feces and urine and vomits. The respirations are slow and labored. The autopsy does not show any signs of so extensive a hemolysis, and the intestinal mucous membrane is much congested and engorged, particularly in the duodenal area.

Not only do the responses seen in the animal vary, but also the pathologic conditions are not the same. A more important point than either of these is the great difference in the minimal lethal dose of the *B. perfringens* toxin as compared to the loop fluid. Generally, from 2 to 5 cc. of the latter, when injected intravenously, results fatally. In the two small dogs just mentioned it required 30 cc. of *B. perfringens* toxin given intravenously to each. The strength of this solution was such that each cubic centimeter contained 2 minimal lethal dose for a pigeon weighing 350 Gm.

Finally, it must be admitted that not only in the isolated loop but also in the obstructed small intestine, *Bacillus welchii* is present. In a bacteriologic study in a few instances, there was a definite increase in the number of these organisms, though the aerobes greatly predominated.

SUMMARY

1. The life of dogs with high intestinal obstruction was not prolonged by the use of *B. perfringens* antitoxin.

2. Evidence is presented to show that a neutralization of the toxic substance or substances contained in isolated intestinal loops is not effected by *B. perfringens* antitoxin in vitro or in vivo.

3. A minimal lethal dose of loop toxin is also fatal to a dog immunized to the toxin of *B. perfringens*.

4. A minimal lethal dose of loop toxin in dogs is decidedly less in amount than that of *B. perfringens*.

5. The hemolysis that follows the intravenous injection of *B. perfringens* toxin into dogs is much greater than that which results from the injection of loop toxin.

6. Dogs may be successfully immunized to the toxin of *B. perfringens*.

CHOLECYSTOGRAPHY

A GENERAL APPRAISAL *

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Prior to 1924, the roentgenologic diagnosis of disease of the gallbladder, in spite of the achievements of a few roentgenologists, was not generally efficient or held in high regard. In that year, Graham and Cole [1] announced their discovery of calcium tetrabromphenolphthalein as a cholecystographic agent. During the four years that have elapsed since then, cholecystography has become indispensable for routine examination, and a voluminous literature testifies to the vivid interest aroused by the new method. Cholecystography has been one of the most remarkable advances in medicine, and, although Abel and Rowntree [2] had previously shown that phenoltetrachlorphthalein was eliminated chiefly in the bile, it was Graham who first applied this principle to visualization of the gallbladder with the roentgen ray.

As the calcium salt proved to be somewhat toxic, Graham soon abandoned it for the sodium salt of tetrabromphenolphthalein. Then Whitaker and Milliken,[3] early in 1925, advocated the use of sodium tetraiodophenolphthalein on the ground that it produced fewer reactions and could be given in smaller doses than the bromine equivalent. Graham had tried the iodine compound almost at the beginning of his work, but because of impurities the drug had proved unsatisfactory. Indeed, he and his co-workers experimented with an impressively long list of compounds before their first publication.

In all the early work with cholecystography, the drugs were given intravenously. In February, 1925, Menees and Robinson,[4] employing the bromine compound, were the first to administer a cholecystographic

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* From the Section on Roentgenology, The Mayo Clinic.

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3. Whitaker, L. R., and Milliken, Gibbs: A Comparison of Sodium Tetrabromphenolphthalein with Sodium Tetraiodophenolphthalein in Gallbladder Radiography, Surg. Gynec. Obst. **40**:17, 1925.

4. Menees, T. O., and Robinson, H. C.: Oral Administration of Sodium Tetrabromphenolphthalein; Preliminary Report, Am. J. Roentgenol. **13**:368, 1925.

substance successfully by mouth, and they were soon followed by Whitaker and Milliken,[5] who reported the oral use of the iodine compound. Attention was then directed to devising satisfactory methods of oral administration and avoiding unpleasant reactions. The drug was given in stearin coated pills, in keratinized capsules and finally in plain capsules. Stewart[6] tried administration through the duodenal tube. Carman and Kendall dissolved the iodine compound in water, precipitated it in colloidal form with citric acid or fruit juices and administered it in the liquid state. While fresh the mixture was palatable and not nauseating, but was so unstable that the experimenters abandoned it without publishing their experience. Diiodocinchophen, brought forward on the Continent in 1926 by Pribram,[7] was given a brief trial in America because of reports that grave reactions had followed its use. In the following year, Kendall and I[8] reported the synthesis and employment of di-iodo-di-ethyl-ether of di-sal-icylphthalein, which proved to be satisfactory, but it is so difficult to produce that it is not available in quantity. Last year, Fantus[9] advocated employment of a colloidal preparation of the iodine compound. Recently, Levyn and Aaron[10] found that this drug can be given in liquid form by dissolving the dose in a small amount of distilled water and adding from 240 to 300 cc. of grape juice. This is not a stable compound, and they recommend dissolving the dose in distilled water and then adding enough malic acid exactly to combine with half of the sodium, thus presumably transforming the unstable di-sodium salt into the stable monosodium salt. This solution can be kept indefinitely and grape juice added before taking. At the Mayo Clinic, more than 500 patients have received 4 Gm. of tetraiodophenolphthalein in simple fresh aqueous solution with instructions to add grape juice and take it after the evening meal.

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5. Whitaker, L. R.; Milliken, Gibbs; and Vogt, E. C.: The Oral Administration of Sodium Tetraiodophenolphthalein for Cholecystography, Surg. Gynec. Obst. **40**:847, 1925.

6. Stewart, W. H., and Ryan, E. J.: Further Development in the Jejunal and Oral Administration of the Tetraiodophenolphthalein Sodium Salt, Am. J. Roentgenol. **14**:504, 1925. Einhorn, Max; Stewart, W. H., and Ryan, E. J.: Experiences with Biloptin (Diiodoatophan); for Cholecystography by Oral or Duodenal Method, M. J. & Rec. **125**:457, 1927.

7. Pribram, B. O.: Ueber ein neues Kontrastmittel zur röntgenologischen Darstellung der Gallenblase, Deutsche med. Wchnschr. **52**:1291, 1926.

8. Kirklin, B. R., and Kendall, E. C.: A New Iodine Compound for Cholecystography, Radiology **9**:205, 1928.

9. Fantus, Bernard: Peroral Administration of Colloidal Contrast Medium in Cholecystography, J. A. M. A. **89**:182 (July 16) 1927.

10. Levyn, Lester; and Aaron, A. H.: Cholecystography by the Oral Administration of Sodium Tetraiodophenolphthalein in Solution, Am. J. Roentgenol. **18**:557, 1927.

Nausea has rarely followed; flocculi of unabsorbed dye are seldom noted in the bowel, and the technic appears to excel any yet proposed for oral administration.

Much discussion has been devoted to the relative merits of the intravenous and oral methods. Graham and his associates,[11] including Sherwood Moore, strongly prefer the intravenous use of the dyes, and employ sodium phenoltetraiodophthalein, the isomer of sodium tetraiodophenolphthalein. Smaller doses of this drug are required, and it serves as a test of hepatic function as well as a cholecystographic medium. Graham and other proponents of the intravenous method felt that the oral method is not reliable unless the result indicates a normally functioning gallbladder, and that otherwise the data should be checked by an intravenous test. They were supported in their views by Case,[12] Blaine,[13] Zink,[14] Boardman,[15] Verbrycke[16] and others. On the other hand, most examiners in America are employing the oral method. While intravenous administration makes it certain that a full dose has been introduced into the circulation and excludes any question of absorption, occasional serious reactions, even in the hands of experts, make one hesitate to urge its use as a general routine. Although the intravenous method is carried out as an office procedure by a few examiners, it is generally held that the patient should be hospitalized; this has the disadvantage of increasing the patient's expense materially. While contraindications to intravenous administration of the dye have been advanced, it would seem from the work of Maddock and Whitaker[17] that contraindications have been overemphasized, especially that of biliary obstruction.

The oral method has no risks or contraindications, and it is easily employed. I have not found records of any serious reaction from its

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11. Graham, E. A.; Cole, W. H., and Copher, G. H.: The Roentgenological Visualization of the Gallbladder by the Use of Intravenous Injections of Sodium Tetrabromphenolphthalein, Radiology **4**:83, 1925. Graham, E. A.; Cole, W. H.; Copher, G. H., and Moore, Sherwood: Cholecystography; the Use of Phenoltetraiodophthalein, J. A. M. A. **86**:1899 (June 19) 1926.

12. Case, J. T.: Some Clinical Aspects of Cholecystography, Tr. Am. Gastro-Enterol. A. **29**:289, 1927.

13. Blaine, E. S.: Personal communication to the author.

14. Zink, O. C.: A Clinical Study of Cholecystitis with the Aid of Cholecystography, Radiology **4**:286, 1926.

15. Boardman, W. W.: The Relative Value of Cholecystography and the Original Lyon Test in Estimating Biliary Tract Function, Am. J. M. Sc. **174**:536, 1927.

16. Verbrycke, J. R., Jr.: Cholecystographic Gallbladder Diagnosis, Tr. Am. Gastro-Enterol. A. **29**:284, 1927.

17. Maddock, S. J., and Whitaker, L. R.: Effects of Sodium Tetraiodophenolphthalein in Complete Biliary Obstruction, Boston M. & S. J. **194**:973, 1926.

use, although nausea, purging or vomiting occur occasionally. Some of the objections urged against the oral method are: (1) the patient may fail to take the drug as instructed; (2) the dye may be vomited shortly after it is taken; (3) its passage into the bowel may be retarded or prevented by pyloric obstruction, and (4) it may fail to be absorbed adequately or at all by the intestine, the fecal content producing dense shadows overlying the gallbladder. Experience indicates that none of these objections is important. At the Mayo Clinic, sodium tetraiodophenolphthalein has been given orally as a routine to thousands of patients during the last three years. For several months a selected group of cases, now numbering more than 200, showing positive data with the oral test, have been checked by intravenous injection. The results, as well as those obtained from similar comparisons by other observers, show that the accuracy of the oral method compares favorably with that reported by partisans of the intravenous technic. Even if a difference in accuracy of 1 or 2 per cent is granted, one is scarcely warranted in insisting on intravenous administration.

DIAGNOSTIC EFFICIENCY OF CHOLECYSTOGRAPHY

Statistics published in America estimate the diagnostic efficiency of cholecystography at from 78 to 100 per cent.[18] Aside from differences due to the personal equation, reasons for the variance will be found in: (1) a lack of exact knowledge as to the line of demarcation between the normal and abnormal gallbladder from the standpoint of the surgeon, anatomist, physiologist and histopathologist; (2) differing conceptions as to cholecystographically normal and abnormal gallbladders; (3) the use or nonuse of clinical data in arriving at cholecystographic diagnoses, and (4) differences in the character of the material on which the computations are based and in the methods of analysis.

According to Judd,[19] surgeons are called on to operate for disease of the biliary tract more often than for any other abdominal lesion, and he considered it of the first importance to determine who shall say whether the gallbladder is diseased, the clinician, surgeon, roentgenologist or pathologist. His expression is fully warranted by the confusion which prevails. While decision whether the gallbladder shall be explored surgically depends primarily on the clinician, he in turn looks to the roentgenologist and surgeon for advice, and all eventually appeal to the anatomist, physiologist and pathologist for basic knowledge. Each link in the chain has its points of strength and of weakness.

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18. Hirsch, I. S., and Taylor, H. K.: A Critical Review of the Röntgenological Diagnosis of Gallbladder Disease, M. J. & Rec. **126**:616, 1927.

19. Judd, E. S.: Cholecystitis, Northwest Med. **25**:167, 1926; **26**:377, 1927.

Thanks largely to cholecystography, the anatomists have learned that, as George [20] pointed out long ago, the gallbladder does not have a fixed position, but, like many other abdominal organs, its form and position vary greatly and are related to habitus. From the physiologist, more exact information is desired as to the functional behavior of the gallbladder and its alteration by nonpathologic states, for the study of which cholecystography itself offers a facile means. Mann [21] and other physiologists considered the gallbladder a rather temperamental organ susceptible of influence by many remote conditions. Mann's work indicates that a degree of stasis occurs during pregnancy. Boyden [22] concluded from his studies that the gallbladders of women empty more quickly than those of men. Plummer,[23] interested primarily as a clinician, observed that a certain type of patient, characterized by easy fatigability, achlorhydria and a low basal metabolic rate, is likely to respond eccentrically to cholecystography, the shadow frequently being faint or absent, although clinical evidence of cholecystic disease is lacking.

More precise definitions of cholecystic disease are needed from the pathologist. It is a moot question whether pericholecystic adhesions necessarily imply a pathologic condition of the gallbladder. Certainly such a gallbladder may concentrate dyes normally, and granting that it is abnormal anatomically, the new question arises whether the abnormality constitutes disease of clinical moment. On the other hand, the capacity of concentrating dye is not invariably diminished by definite disease, nor is there a constant relation between the degree of concentration of bile and that of cholecystographic media, as shown by Caylor, Bollman and myself.[24] The significance of petty anatomic changes which are visible only with the microscope is also open to argument. In many instances the changes, which have conveniently been designated as "cholecystitis graded 1," signifying cholecystitis of minimal degree, possibly represent ancient disease now healed or quiescent; in other instances, abnormalities of equal extent are meaningless, and the gall-

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20. George, A. W., and Leonard, R. D.: The Pathological Gallbladder, New York, Paul B. Hoeber, 1922, vol. 2, pp. 143.

21. Mann, F. C.: A Physiologic Consideration of the Gallbladder, J. A. M. A. **83**:829 (Sept. 13) 1924; The Physiology of the Liver and the Gallbladder, Minnesota Med. **11**:25, 1928. Mann, F. C., and Higgins, G. M.: The Effect of Pregnancy on the Emptying of the Gallbladder: A Preliminary Report, Arch. Surg. **15**:552 (Oct.) 1927.

22. Boyden, E. A.: Sex Differences in Contraction Rate of Human Gallbladder, Proc. Soc. Exper. Biol. & Med. **24**:353, 1927.

23. Plummer, H. S.: Personal communication to the author.

24. Kirklin, B. R.; Caylor, H. D., and Bollman, J. L.: The Concentration of Cholecystographic Mediums and Bilirubin by the Gallbladder, Radiology **9**:463, 1927.

bladder can be rated as normal. It is an odd fact that most patients with cholecystitis graded 1, who have at any time had marked symptoms suggestive of cholecystitis, profit by cholecystectomy, while most of such patients whose symptoms are slight and atypical do not derive benefit from the operation. Obviously there is a point at which even the microscope fails to distinguish with certainty between health and disease, or at least fails to throw light on the clinical import of slight departures from the normal.

The warmest advocates of cholecystography have no reason to complain of the general attitude of clinicians toward the method, for few of the latter have offered criticisms of the procedure. Eusterman,[25] however, insisted that the roentgenologist should never assume the responsibility of diagnostician, valuable as the aid of the x-ray may be, and asserted that it is out of harmony with medical experience to expect cholecystic disease to be diagnosed infallibly by any single laboratory test.

In view of the basic defects in knowledge of the function and pathologic changes of the gallbladder, it is surprising, not that cholecystography is sometimes in error, but that it is so rarely wrong, and that the distinctions between normal and abnormal responses to the test as first laid down by Graham should be maintained with so little alteration. However, individual examiners vary considerably in their application of these criteria and in stringency of interpretation. For my own part, I am constantly inclined toward a more liberal appraisal of the normal and a more conservative judgment of the abnormal. This attitude is in consonance with the fact that cholecystography is a test principally of the dye-concentrating ability of the gallbladder and, except in patients with stones, not a means of demonstrating pathologic changes directly. Further, it is a test of function at the moment, without any obligatory relation to previous disease or future recurrences. In my own work, it is the custom to construe the cholecystographic data without any knowledge of the clinical facts in the case. Acquaintance with the clinical history may assist the examiner in making diagnoses when the roentgenologic evidence is scanty or equivocal, but such diagnoses are not roentgenologic. Eventually, all the facts from all sources should be weighed together, but this correlation belongs properly to the clinician.

Perhaps the most difficult item of cholecystographic interpretation is the determination of what constitutes normal density of the cystic shadow. Density not only varies with the drug employed and the quantity prescribed but has a considerable range of variance under

25. Eusterman, G. B.: Limitations of Cholecystography with which Physicians Should be Familiar, J. A. M. A. **90**:194 (Jan.) 1928.

comparable conditions, and the personal equation enters inevitably into judgment. The density is seldom of the ideal quality depicted in published illustrations. Ordinarily, the shadow is denser at the sixteenth hour than at the fourteenth; at the twentieth hour, a fatty meal having been taken in the meantime, the shadow will most often have disappeared. But the sequence is not inflexible, and the shadow may be densest at any one of the three periods. As a rule, the shadow will be slightly larger at the second period than at the first, although the reverse is sometimes true; here, again, the sequence is less important than the fact of changing size. In asthenic persons the gallbladder is likely to be long, slender and perhaps pointed; in the sthenic or hypersthenic habitus, it is usually short and rounded; exceptions are numerous, and the general form is without significance. Its position is widely variable, and it may be seated high or low, mesially or laterally, without meaning. The shadow should be homogeneous in the sense of not having persistent thin areas or dense spots, although a higher concentration of dye at the fundus is common during the final stage of emptying. On the whole and with few exceptions, judgment of any particular quality of the shadow should be based, not on its worst, but on its best, appearance at any stage of the examination.

INDICIA OF CHOLECYSTIC DISEASE

After four years' experience, observers differ, of course, as to the value of the various signs of disease, and it would be difficult to summarize general opinion. I shall therefore emphasize only those signs which I have found trustworthy.[26] If one assumes that lapses of technic can be excluded, the reliable indicia of cholecystic disease comprise but three varieties of abnormality in the shadow of the gallbladder: (1) absence of shadow, (2) faintness of the shadow and (3) mottling of the shadow. Although absence of a shadow may result from extensive disease of the liver, failure of the dye to be absorbed by the intestine, or defects in the mechanism regulating the bile pressure, experience has proved such causes to be rare, and this negative sign can be construed consistently as an index of disordered function. I would insist strongly on the necessity of caution in pronouncing the shadow to be faint, for normal concentration has a wide latitude, and only a shadow which is scarcely visible at all periods can safely be considered faint. Mottling of the shadow, by either denser spots or translucent areas, is significant of stones when superposed intestinal gas, calcified glands, ossifying costal cartilages or transverse processes can be barred. If the gallbladder remains unchanged in size throughout,

26. Kirklin, B. R.: Efficiency and Limitations of Cholecystography, Boston M. & S. J. **197**:1487, 1928.

especially if the shadow is constantly faint, the patient should be reexamined without dye, for in such instances the shadow may result from disease of the gallbladder and not from drug-laden bile.

Irregularities of contour seldom denote intrinsic disease. A marked serration of the border, the shadow being fixed in position and in the same situation at all periods, has been seen rarely in cases showing dense adhesions, and a single band of adhesion may produce an incisura with hour-glass deformity of the gallbladder. As the function of concentration is preserved, the gravity of the condition is doubtful and its cholecystographic manifestation is rare, for in most instances adhesions, however dense, do not cause deformity of contour. Angulation at the neck of the gallbladder has no pathologic import. The large or small size of the gallbladder is without significance. Occasionally the cystic shadow does not appear until the twentieth hour, but on reexamination the cholecystograms almost invariably follow the usual sequence, so that the delayed appearance of the shadow was probably due to the patient's failure to comply with instructions. While further experience may prove that delayed filling and its opposite, retarded emptying, are indicative of disease, I have not yet been able to attach importance to either alone.

Since cholecystography is preeminently a test of the ability of the gallbladder to receive and concentrate dye-laden bile and since this capacity does not have a constant relation to health or disease, it would seem that the examiner's report to the clinician should be in terms of function rather than of anatomic condition. Accordingly, at the Mayo Clinic reports are now made in one of three forms: (1) normally functioning gallbladder, (2) poorly functioning gallbladder, when the shadow is persistently faint, and (3) nonfunctioning gallbladder, when a shadow of the viscus is not seen. Evidence of stones may be associated with any of the three types and is so reported.

Differences in material and in methods of analysis undoubtedly account for some of the divergent statistics regarding the accuracy of cholecystographic diagnosis. For example, Graham's and Sherwood Moore's computations, as the authors have been careful to point out, have been based on one group only, those cases in which the cholecystographic data indicated disease and the gallbladder was removed at operation. Their estimate of 97 per cent accuracy is not extravagant and agrees substantially with the results in this group at the Mayo Clinic and elsewhere. This percentage cannot be taken, however, as indicating the average efficiency of cholecystography, since account is not taken of cases in which the cholecystographic symptoms are normal and the ratio of error is highest. Complaint has been made also that high valuations of cholecystography occasionally have been based on a small series of cases. Yet when analyzed on similar bases, the statistics are not really

discordant. They are highly complimentary to the method, and experience at the Mayo Clinic may be cited as probably representative.

Cholecystography at the Mayo Clinic has increased progressively in accuracy during the last three years. During that time, there were 17,289 examinations with 2,476 patients operated on. In 1925, the general accuracy of all cholecystographic diagnoses, including those on normal persons, was 79 per cent; in 1926, it was 84 per cent, and in 1927, 90 per cent.

During 1927, 5,705 patients were examined. In 1,967 (34.4 per cent) the cholecystographic data indicated disease, while in 3,738 the data pointed to a normally functioning gallbladder. Of the whole number of patients examined, 869 were operated on, either for disease of the gallbladder or for an abdominal lesion. Among the 869 patients with and without cholecystic disease, cholecystography had forecast the condition found at operation in 778 (90 per cent).

Conditions reported by the surgeon or pathologist were as follows: diseased gallbladder with stones, 422; diseased gallbladder without stones, 147, and other abdominal lesions, 300.

In 97 per cent of 422 cases in which gallstones were found, the cholecystograms indicated a poorly functioning or nonfunctioning gallbladder. In only 170 cases (40 per cent) were gallstones manifest as dense or translucent areas and diagnosed as stones.

Of the 147 cases in which the gallbladder was diseased but did not contain stones, there was evidence of disturbed function in 100, while in 47 the gallbladder was apparently deporting itself normally.

Among the 300 cases in which the gallbladder was pronounced normal by the surgeon and pathologist, cholecystograms were normal in 90 per cent.

To analyze the 869 cases from the standpoint of the various types of roentgenologic data, the series may be divided into four groups: (1) nonfunctioning gallbladder with and without stones, (2) poorly functioning gallbladder with and without stones, (3) normally functioning gallbladder with stones and (4) normally functioning gallbladder without stones.

In the first group were 317 cases in which the gallbladder was reported to be nonfunctioning. In 243 of these (76.6 per cent) the diseased gallbladder was found to contain stones at operation; in 57 (18 per cent) the gallbladder was diseased but did not contain stones, and in 17 (5.4 per cent) the gallbladder was considered normal by the surgeon or pathologist or by both. In short, in 95 per cent of the cases of nonfunctioning gallbladder the condition was confirmed at operation.

In the second group were 212 cases in which the gallbladder functioned poorly. In 156 of these (73.6 per cent) cholecystic disease

with stones was found at operation; in 43 there was definite disease of the gallbladder but no stones, and in thirteen the gallbladder was normal. The total accuracy of diagnosis in this group was 94 per cent.

In the third group were 9 cases interpreted as showing a normally functioning gallbladder with stones, in all of which the condition was confirmed at operation.

In the fourth group, in which a normally functioning gallbladder was reported, there were 331 cases, and it is in this group that the highest percentage of error occurred. At operation the gallbladder was pronounced normal in 270 cases, but in 47 it was definitely diseased, and in 14 others it contained stones. When the films were reviewed, a few instances were found in which the patient had moved or the films were of substandard quality so that by reexamination stones might have been discovered, but in most of them, as well as in the cases showing diseased gallbladder, there was no reason to change the original roentgenologic diagnosis. That the normal cholecystogram should be relatively less reliable than the abnormal is contrary to general expectation. It is compatible, however, with the work of Caylor and Bollman,[27] who have shown that the function of concentrating bile may be preserved or even enhanced in spite of advanced disease of the gallbladder. They have shown that in certain types of cholecystic disease the entire organ is not necessarily involved; there may be hyperfunctioning areas, impaired areas and normal areas.

In addition to the foregoing analyses, I have reviewed the cases showing positive cholecystographic data in which the gallbladder was later removed. It is on a similar group that Graham's figures are based. Among the 505 cases in this group, 496 showed gross evidence of cholecystic disease, while nine showed only microscopic changes indicating a mild cholecystitis. If one assumes for the sake of accurate statistics that these nine cases represented normal gallbladders, the accuracy of diagnosis in this group was 98.2 per cent. In all of these cases, the drug was given orally.

SUMMARY

While no one can speak with full authority as to the present status of cholecystography in America, the following might be regarded as outstanding features:

1. Notwithstanding its brief history, cholecystography has attained unusually wide vogue and has achieved a diagnostic excellence equal or superior to that of accepted tests for other diseases.

2. The method is so efficient already that further improvement will probably be gained only slowly and by strenuous effort. Lines along

27. Caylor, H. D., and Bollman, J. L.: Bilirubin Content in Gallbladder Bile in Cholecystic Disease, Arch. Path. **3**:993 (June) 1927.

which advance may lie include the development of new cholecystographic compounds and improved technic of examination.

3. Like all laboratory tests, especially those applied with the x-ray, the greatest misfortune to cholecystography has been, not the scant criticism it has received, but the tendency to credit it with infallibility and to depend supinely on its verdicts.

4. In spite of the general efficiency of cholecystography, it has its limitations and is subject to errors of interpretation many of which will probably continue to be inevitable. Fear has been expressed that by erroneous diagnoses of disease the test will be made a pretext for unwarranted operations. Yet it is equally objectionable to make a normal cholecystogram the pretext for failure to operate when operation is indicated, and the negative diagnoses furnish the greater percentage of errors.

5. A keener realization that the diagnosis of cholecystic disease is ultimately a function of the clinician and not of cholecystography or any other laboratory test is urgently to be desired at home and perhaps abroad. Cholecystography is a remarkably able coadjutor, but, whatever it may reveal, the clinician cannot forsake his prerogative and duty to correlate the data with his own information, weigh the probabilities of disease, estimate its gravity and recommend appropriate treatment.

THE RELATIVE EFFECTS OF DISTENTION ON DIFFERENT PORTIONS OF THE INTESTINE*

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One important clinical and experimental observation has long been accepted, namely, that acute obstruction in the proximal small bowel, duodenum or jejunum is more rapidly followed by serious symptoms and death than acute obstruction lower down, in the ileum or the colon. This has been variously explained. It has seemed possible to various workers that in addition to other possible factors, this might be correlated with the susceptibility of the wall of the bowel to interference with its circulation by the distention usually resulting from the obstruction. Some years ago, we [1] stated:

> Organs, such as the colon or stomach, which have in part a storage function are capable of very great distention without injury by reason of the arrangement of their blood supply. On the other hand, the small intestine, especially the duodenum, is capable of practically no dilatation. By reason of its investment in a tough, fibrous envelope and the position of its nutrient vessels, which are arranged parallel to its long axis, any distention of the duodenum must result in an immediate circulatory damage.

In a recent paper, Foster [2] stated:

> In high level lesions the course is more rapid and severe because the intestine here has a high degree of irritability and distention is more rapid. Because of the anatomic construction of this area, necrosis appears more quickly from secretion and internal pressure.

It seemed to us that, in part at least, these explanations might be subjected to experimental demonstration.

Many writers at various times have referred to the seemingly obvious disturbance of circulation in the bowel wall accompanying distention. A few workers have made special studies on this problem and have brought out various significant facts.

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* From the Department of Physiology and Pharmacology of Northwestern University Medical School.

1. Dragstedt, L. R., and Dragstedt, C. A.: Acute Dilatation of the Stomach, J. A. M. A. **79**:612 (Aug. 19) 1922.

2. Foster, W. C.: Acute Intestinal Obstruction, J. A. M. A. **91**:1523 (Nov. 17) 1928.

Van Zwalenburg,[3] in 1907, made certain observations on the blood flow in the bowel wall by means of a light within the lumen of the intestine. He observed that with distention of the intestine by a pressure of 30 mm. of mercury some capillary streams were arrested; at 60 mm., small veins were arrested, and in most veins the current was slow; at 90 mm., all blood streams were moving slowly, and many but not all currents were changing direction frequently; at 130 mm. pressure, all circulation ceased, and there was some oscillation of corpuscles but no progress. He concluded:

> The demonstration seems complete that distention of the gut (or of other hollow viscera) interferes with the circulation in its wall, and allows infiltration and effusion to take place into its walls and lumen and any other open spaces which may come within its influence. The return circulation is retarded at comparatively slight pressures. Effusion follows, as in all obstructions to venous flow. As the average venous pressure in the intestine under ordinary circumstances probably varies from 4 to 10 mm. of mercury, any pressure beyond that will offer some resistance to the return current.

In 1926, van Bueren [4] studied the pathologic changes occurring in distended loops of bowel and found that the characteristic features were areas of hemorrhagic infarction on the antimesenteric surface of the intestine, with varying degrees of necrosis to perforation occurring in these areas depending on the duration of the distention.

In 1927, Gatch, Trusler and Ayers [5] studied the effect of intestinal distention on the circulation of the bowel by recording the effect of such distention on the rate of blood flow in the returning veins. Their observations in general were confirmatory of van Zwalenburg's, but, in addition, afforded an estimate of the degree of circulatory impairment at different levels of pressure.

In none of these reports, however, is there any reference to the comparative effects that may occur in different portions of the bowel to the same pressures. In most instances there is no reference as to which portion of the bowel was used for the experiment. We have accordingly endeavored to compare by a variety of methods the effects of distention at different pressures on the circulation in the bowel, using for this purpose the duodenum, terminal jejunum to proximal ileum and the colon. Dogs were used in all the experiments.

Several experiments were performed by a method similar to that of Gatch, Trusler and Ayers, except that water pressure was used instead

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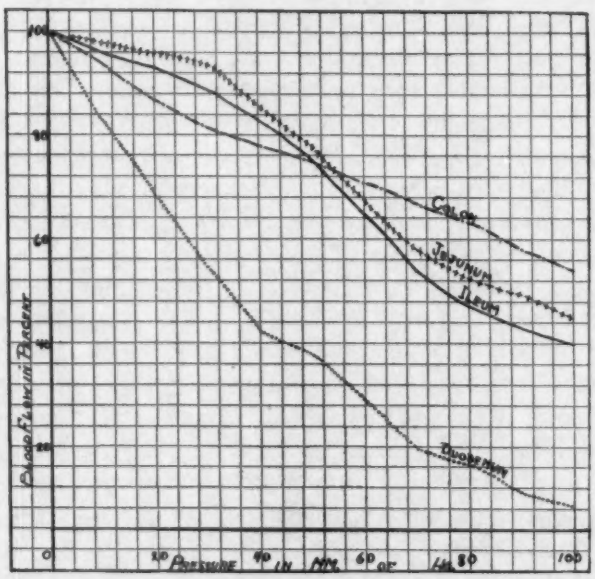
3. Van Zwalenburg, C. V.: Strangulation Resulting from Distention of Hollow Viscera, Ann. Surg. **46**:780, 1907.

4. Van Beuren, F. T.: The Mechanism of Intestinal Perforation Due to Distention, Ann. Surg. **83**:69, 1926.

5. Gatch, W. D.; Trusler, H. M., and Ayers, K. D.: Effects of Gaseous Distention on Obstructed Bowel, Arch. Surg. **14**:1215 (June) 1927.

of gas pressure, and heparin was used to prevent coagulation of blood. Under anesthesia, a loop of duodenum, of the lower jejunum or upper ileum, and of the colon were isolated, cannulas inserted into the main vein draining the loop and the lumen of the loop connected to the pressure bottle. In this way simultaneous determinations of changes in the venous flow from the three loops induced by changes in intra-enteric pressure could be determined. The results of ten observations on four dogs are shown graphically in the accompanying chart in which the venous return is expressed in the percentage of the original control rate of flow. It is shown clearly that increasing distention produces an increasing impairment of the venous return in all instances, but that the



Effect of intra-enteric pressure on intestinal circulation.

circulation of the duodenum is much more profoundly affected than any other portion of the bowel. Our results with the jejunum and ileum check closely the results of Gatch, Trusler and Ayers, and lead us to believe that the small intestine used by them in their experiments was either the jejunum or the ileum and not the duodenum. We were also able to corroborate their observation that there is a residual flow of somewhat varying amounts which no amount of intra-enteric pressure stops. This appears to be due, as they stated, to anastomotic vessels in the mesentery. It was our experience that prolonged distention gradually increased this flow of blood through the anastomotic vessels until it nearly equalled the original flow. Thus even when the entire intestine from the pylorus to the anus is distended at sufficient pressure

to prevent all blood flow in the intestinal wall, the volume of blood flowing into the portal vein seems to return nearly to its original amount.

Four experiments of the type used by van Zwalenburg were also performed. Loops of different portions of the bowel were prepared and connected to a pressure bottle and manometer. A small cystoscopic electric light was inserted into the lumen through a small incision kept tightly closed by a purse-string suture and the vessels in the bowel wall watched with the aid of a hand lens and low power microscope. In three dogs it was found that the flow in the veins of the lateral wall of the intestine ceased in the case of the duodenum at a distention pressure of from 35 to 40 mm. of mercury, in the case of the jejunum and the ileum at a pressure of from 55 to 65 mm. and in the case of the colon at 95 mm. In the fourth dog the respective pressures required were 65, 95 and 140 mm. Thus, although considerable variation seemed to occur in the actual pressure required, in every instance the flow in the vessels of the duodenum was impaired at lower pressure than that required for the rest of the intestine. It was also apparent from these observations that the obstruction to the flow occurs in the wall of the intestine as suggested by van Beuren, and not in the adjacent mesentery.

A number of attempts were made to demonstrate the effect of distention on the intestinal circulation by injecting into the circulation (both intravenously and intra-arterially) various dyes, lamp black and India ink, after first distending the intestines to various pressures. No clearcut effects were noted, and no conclusions drawn. Varying degrees of staining were not readily detected. Complete absence of staining appeared only when distention pressures were sufficiently high to occlude the arterial supply. Staining seemed to be equally marked both when there was no distention and when distention was of sufficient degree to impair the venous return.

The previous observations were generally in accord that the duodenal circulation was more susceptible of impairment than that in the jejunum and ileum, and that in the jejunum and ileum more so than the colon. Three groups of experiments were then performed to see if corresponding pathologic changes could be produced demonstrating the same gradation of effect by maintenance of the pressure over fairly long time intervals. In the first group of eleven animals, the pylorus and anus were tied, and the entire intestine distended at a constant pressure, the anesthesia being maintained. At the end of the experiment the different portions of the intestine were examined and compared. The results are indicated briefly in table 1 in which the outstanding circulatory changes are graded according to degree. During the course of some of these experiments, incisions were made in the wall of the bowel at various places to note the hemorrhage. This was done to note the effect on arterial flow. It was frequently observed that at a given

pressure, with the doudenum pallid and the jejunum or ileum hyperemic, freed bleeding would occur in the latter with no bleeding from the duodenal wall.

In the second group of seven animals, the pylorus was tied off, the anus closed by double string suture and the entire intestine distended with mineral oil. The abdomen was then closed and the animal allowed to recover from the anesthetic. All of the animals died in from ten to forty-eight hours except two in which leakage at the anus had occurred and abdominal distention had disappeared. In the other animals, the entire intestine was dilated, but there was no material pressure in the lumen. It was apparent, of course, that at whatever pressure injected the pressure would fall practically to zero as soon as any loss of tone or relaxation of intestinal musculature occurred. In two of the

TABLE 1.—*Effect of Intestinal Distention of the Bowel Wall*

			Duodenum				Jejunum-Ileum				Colon			
Exper. No.	Pressure In Mm. Mercury	Duration Hours	Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infarct	Pallor
19	50-55	4½	+++	0	++	0	0	+	0	0	0	0	0	0
26	55-60	11	++	0	0	+	0	+	0	0	0	0	0	0
27	60-65	8½	+	0	0	++	0	+	++	0	0	+	0	0
10	65-70	3	+++	0	0	0	0	+	0	0	0	0	0	0
11	65-70	4	+	0	0	0	0	0	0	0	0	0	0	0
12	65-70	5	0	+	+	0	0	+	0	0	0	+	0	0
13	70-75	2	0	0	0	++	0	++	0	0	0	0	0	0
23	70-75	7½	0	0	0	++	0	++	++	0	0	+	0	0
24	70-75	3	0	0	0	++	0	++	++	0	0	+	0	0
17	75-80	8	0	0	+	+	0	0	+	0	0	+	0	0
18	75-80	8	0	0	+	+	0	0	+	0	0	+	0	0

animals there was a marked pallor of the duodenum contrasting with a condition of marked hyperemia and hemorrhagic infarction in the jejunum and ileum, and an approximately normal condition of the colon. In the other three animals, there was no great difference between the different portions of the bowel.

In the third group of animals, the experiment was performed as in the second group except that the intestinal tract was distended with nitrogen using different initial distention pressures. It was felt that owing to the slow disappearance of this gas from the intestinal lumen, a continuous distention pressure would be maintained until the death of the animal. Even with a slight amount of absorption or leakage the pressure would fall but gradually. The results are indicated in table 2 in which again the main changes in the wall of the bowel are graded according to degree.

From these three groups in which the pathologic changes produced by prolonged distention at various pressures were studied, the following

observations seem warranted. At a certain low, apparently minimally effective pressure, varying degrees of circulatory damage from cyanosis to hemorrhagic infarction may be produced in the duodenum with little disturbance elsewhere. As the pressure increases, these same changes begin to become manifest in the jejunum and ileum, but are accompanied by pallor and anemia in the duodenum. With further increase in pressure these evidences of circulatory damage begin to become prominent in the colon, while anemia and pallor begin to appear in the jejunum and ileum. With still greater pressure it would appear that anemia and pallor would prevail throughout the intestine. These observations are in consonance with those in the preceding experiments and seem to indicate that the circulation, both arterial and venous, is more vulnerable to the effects of distention in the duodenum and progressively less so as the rectum is approached.

TABLE 2.—*Effect of Prolonged Gas Distention on the Bowel Wall*

			Duodenum				Jejunum-Ileum				Colon			
Exper. No.	Initial Pressure	Duration Hours	Cyanosis	Hyperemia	Hemorrhagic Infaret	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infaret	Pallor	Cyanosis	Hyperemia	Hemorrhagic Infaret	Pallor
44	2#	18	0	++	++++	0	0	++	+	0	0	+	0	0
45	2#	24	0	++	0	0	0	+	0	0	0	0	0	0
			Leak with loss of pressure											
46	2#	30	0	++++	++	0	0	++	0	0	0	0	—	0
											(Appendix only)			
47	3#	23	0	++	0	+	0	++	0	0	0	+	0	0
48	4#	10	0	0	++	++	0	++	+++	0	0	+	++	0
											(Appendix only)			
49	5#	12	0	0	0	+++	0	0	0	++	0	++	++++	0

There appears to be an anatomic explanation for this difference in susceptibility according to the demonstration by Eisberg[6] that in the small intestine the vasa recta pierce the muscularis in the mesenteric quarters, while in the large intestine they pierce the muscularis in the antimesenteric portion. According to some preliminary studies that we have made on the dog's intestine, the location at which the vasa recta pierce the muscularis in the jejunum and the ileum is approximately midway between the arrangement in the duodenum and that in the colon. That is to say, that if we represent the cross-section of the bowel by the face of a clock with the mesenteric attachment at 6, the vasa recta pierce the muscularis in the case of the duodenum at approximately 5 and 7, at 3 and 9 in the case of the jejunum and ileum and at 2 and 10 in the case of the colon. The superficial disposition of the vessels seem to allow them to withstand better a certain amount of distention without interference with the respective blood flow.

6. Eisberg, H. B.: On the Viability of the Intestine in Intestinal Obstruction, Ann. Surg. **81**:926, 1925.

CONCLUSIONS

1. Distention of the intestine interferes with the flow of blood in the vessels in its wall.

2. This interference is greatest in the doudenum and least in the colon.

3. This variation in susceptibility appears to be correlated with a variation in the distribution of the blood vessels in the wall of the intestine.

WHAT IS OPERATIVE MORTALITY?*

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"Operative mortality" is a term frequently encountered in surgical literature and used, apparently, to include the proportion of deaths which occur soon after operations. The reports of the percentage of deaths which quickly follow operations and which are regarded as operative mortality vary so widely for the same operation by different surgeons that it is evident that there has been no attempt to standardize the expression nor to explain its meaning or inclusion. Some writers report "hospital mortality," and others simply "mortality"; the former is definite, the latter undefined.

Some variation in operative or in a definite chronologic mortality may be expected, but great variations should be explained as Jones has done [1] with Miles' reports on operations on patients with cancer of the rectum in whom the mortality varied from 9 to 36 per cent, depending on the mode of anesthetization. The operative mortality will, of course, depend on and vary directly with the proportion of cases which the surgeon regards as operable. It is also true that classes of patients vary, and one hospital may not receive patients from the same social stratum that patronizes another hospital. One class of patients delays seeking surgical assistance more than another, thereby increasing the danger of the development of complications and their earlier fatal consequences. The questions of racial and national characteristics of patients are factors. It seems unjust, therefore, to draw comparisons between different operators by their undefined figures alone. In reporting early operative mortality some brief explanations, including the complicating conditions which hasten death, would assist in determining the preferable treatments to be applied to the given diseases. Nonoperable cases in which exploratory operations are performed should, of course, not be listed with the others, but studies of this type of case are desirable to determine better methods for earlier diagnosis and more effective means to secure the patients at earlier dates.

Hospital mortality and the total mortality in cases of cancer are slightly suggested by the results of some combined figures of all Philadelphia and Pittsburgh hospitals for 1927: cancer of the stomach, 37 per cent deaths in the hospitals; cancer of the breast, 13 per cent,

* Submitted for publication, Jan. 23, 1929.

1. Jones, D. E., in discussion on Rankin, Fred: Colostomy and Posterior Resection for Carcinoma of the Rectum, J. A. M. A. **89**:1965 (Dec. 1) 1928.

and cancer of the uterus, 13 per cent. The total number of deaths from cancer in these two cities that same year would raise the total mortality to 98 per cent for cancer of the stomach, 42 per cent for cancer of the breast and 35 per cent for cancer of the uterus; the last figures are irrespective of operation, as all death certificates do not state definitely whether an operation had been performed.

Postoperation mortality, which is not operative mortality, shows wide variations, as stated by Saltzstein [2] in a survey showing operative mortality after resection of the stomach to be from 27 to 46 per cent, after rectal resections from 27 to 49 per cent, after operations for abdominal cancer 40 to 50 per cent, with minimum figures down to zero after operations for cancers of the breast, 7 per cent after operations for gastric cancers and 3 per cent following those for cervical or rectal cancers.

To determine the postoperative length of life the original death certificates of persons dying of cancer during 1927 in Pennsylvania were consulted. The dates of operation are not always supplied as they should be. In this series of cases, patients having a single operation and those in whom the operation was a definite operation for a single organ were selected. Intestinal and hepatic cases were excluded. The list includes patients operated on for cancer of the esophagus, stomach, pancreas, rectum, breast, bladder and generative organs. There was a total of 1,079 deaths; 436 occurred within the first month and 878 within the first year. In the succeeding five years there were 88, 51, 21, 13 and 13 deaths, respectively. Forty-six, or 4.3 per cent, of the patients lived over three years, and 15, or 1.4 per cent, over five years. Collectively, the deaths occurring during the first four weeks after operation numbered 276, 85, 54 and 21, respectively. There were 42 deaths occurring the same day as the operation. The number of deaths each succeeding day during the first week were: 46, 46, 31, 39, 30, 20 and 23. The second week the number of daily deaths were: 19, 9, 12, 8, 13, 7 and 17.

These figures show that the mortality following operation for cancer was greatest during the first year, during the first month and during the first week: 26 per cent of the deaths occurred in the first week and 8 per cent within twenty-four hours.

Complicating conditions that appear to have a direct connection with the operation were recorded for 114 of these cases in which deaths occurred from cancer within a week of the operation. These conditions included acute heart failure in 21 cases, acute intestinal obstruction in 21, postoperative pneumonia in 20, shock in 16, peritonitis in 12,

2. Saltzstein, Harry C.: The Average Treatment of Cancer, J. A. M. A. **31**:465 (Aug. 18) 1898.

uremia and hemorrhage in 6, embolism in 3, acute gastric dilatation in 1, acute urinary suppression in 1 and thrombosis in 1. Such conditions, I believe, can be regarded as operative complications, due to and following operation. There were 86 other deaths with defined complications in hopeless cases in most of which the operations occupied but minor positions in hastening death. These complications included metastases and extensions, grave organic conditions in the heart, kidneys or other organs, diabetes, toxic goiters, anemia, toxemia, cachexia or senility. In most of these instances the laparotomy was only exploratory. Operation was not necessarily contraindicated in any of these cases, as there was at least some chance of helping the patient.

A consideration of some individual organs and the immediate causes of death in connection with them is worth while. Those organs on which the greatest number of operations were required were the stomach, pancreas, uterus, bladder, prostate, rectum and breast.

The stomach with the pyloris was represented in 277 dated operations for carcinoma. The first four weeks 90, 26, 20 and 7 patients died, totaling 143. Twenty-three died within the next month, 21 within the third, and so on. One-half the patients died within a month after operation: 49, or 17.6 per cent, lived six months or longer; 21 lived one year or longer; 10 lived two years or longer, and only 2 lived over four years, then died. There were 12 deaths the day of operation, 82 within the next seven days, 26 within the second week and only 14 the third week. The deaths within the first week were 34 per cent of the total. These few figures do not indicate the relative mortality following these operations for cancer, but do suggest how soon fatalities may occur.

The complications recorded with the cases of gastric cancers in which deaths occurred in the first week comprised the following conditions, which may be regarded as directly related to the operation: shock in 3 cases, hypostatic pneumonia in 7, acute myocarditis in 12, acute obstruction in 5, acute gastric dilatation in 2, uremia in 2, peritonitis in 4 and hemorrhage in 1, a total of 36 postoperative complications giving a mortality ratio of 13 per cent. The other complications with extensive metastasis and distinct inoperable conditions for which the laparotomy was exploratory in nature, included chronic myocarditis, nephritis and diabetes, and included 24 cases in which no complicating conditions were recorded on the death certificates. The extended metastases and organic degenerations had no connection with the operation which was done as a last resort in a hopeless case, but because of the 24 undefined cases the operative mortality resulting from these gastric cancers cannot be placed at 13 per cent for these operators.

Pancreatic postoperation deaths from cancer totaled 64; 30 occurred during the first week; 52 during the first three months, and none after

the tenth month. Acute cardiac dilatation, shock, perforation, intestinal obstruction, hemorrhage and peritonitis accounted for 15 of the 30 deaths during the first week; in 9 other certificates complications were not defined. Thirteen of the 30 deaths occurred within the first twenty-four hours after operation. Some of these laparotomies were diagnostic.

Deaths from uterine cancer, including cervical cases, numbered 98; 10 occurred on the day of operation, and 42 during the first week. Thirty-seven women lived over one year; 19 lived over two years; 7 lived over three years, and 2 died after six years. Shock in 4 cases, and hemorrhage, peritonitis, acute cardiac failure, uremia and suppression of urine accounted for 10 of the 19 defined complications occurring in early deaths. Twenty-three of the 54 deaths resulting from cancer of the ovary occurred during the first week after operation, acute heart failure accounting for half of the eight operative deaths. Twenty-nine of the patients with ovarian conditions died the first month after operation; 45 died the first year; 5 died the next year, and only 2 of 54 patients lived five years.

Prostatic cancer was represented by 68 patients dying postoperatively. Fourteen of these died the first week, 11 the second week and 32 more within six months. Seventy-three per cent of the patients died within six months, and 12 per cent lived a year; only two patients lived over two years. During the first week, shock and intestinal obstruction caused 5 deaths; acute myocarditis, toxemia and peritonitis each were the cause of a death.

Cancer of the rectum accounted for 106 deaths in this list of cases in which operation had been performed; 35 patients died within the first week after operation; 6 the second week, and 8 the third week. Forty-four died within the first six months, and 15 within the second six months. Fourteen, or 13 per cent, lived, but half of these died within a year; the remainder died within eight years. The immediate causes of 35 deaths occurring during the first week after operation included intestinal obstruction in 10, pneumonia in 5, perforation in 2, peritonitis in 2, shock in 1 and undefined complications in 8. These figures indicate a great risk from operation.

Cancer of the breast shows a much lower early mortality than any of the other cases herein listed. In a total of 210 postoperation deaths only 12 occurred the first week, and 26 the first month. During the first year 112, or 41 per cent, died; 38 died the next year, and 26 the third year. Twenty-six, or 12 per cent, lived more than three years, and 3 per cent over five years. One death occurred eleven and 1 twelve years after operation, and another cause of death was recorded as "carcinosis" thirty years after amputation of a cancerous breast. The causes of the deaths during the first week were acute cardiac dilatation,

pneumonia, cerebral embolus, shock, toxic goiter, apoplexy, chronic myocarditis and dementia.

The percentage of deaths occurring within the first week following operation was as follows: 29 from cancer of the stomach, 52 from cancer of the pyloris, 48 from cancer of the esophagus, 48 from cancer of the gallbladder, 47 from cancer of the pancreas, 6 from cancer of the breast, 17 from cancer of the uterus, 42 from cancer of the ovary, 9 from cancer of the bladder, 20 from cancer of the prostate and 33 from cancer of the rectum. These are not representative ratios because the number of cases in this report are so few, but they do suggest high immediate mortality for some operations for cancer and low mortality for others. If operative mortality is considered to include only deaths resulting from shock, postoperative pneumonia, hemorrhage, peritonitis, acute myocardial collapse, acute intestinal obstruction, urinary suppression and similar conditions having a direct bearing on or resulting from the operation, the operative mortality of these cases of cancer would be much lower than these figures, but they cannot definitely be determined from the incomplete death certificates, a considerable number of which name no complications and give no idea whether the cases were found to be inoperable or whether the operation had a direct bearing on hastening death.

These cases of cancer are far too few to establish a general chronologic mortality rate, but they do suggest certain conditions resulting from the operative work of a large number of surgeons. In no way do they indicate the mortality ratio of these operations. There is no definite way in a state survey to approach this important item. For instance, the Pennsylvania hospitals in a questionnaire reported admitting 1,065 patients with cancer of the breast during 1927, with 80 deaths resulting in the hospitals, and the state mortality records show 852 deaths from malignant conditions, 810 from cancer of the breast, but because of the incompleteness of the death certificates the number of these patients on whom operations were performed cannot be determined.

The chief object in mentioning in a surgical paper the operative mortality following some specific disease or operation is to determine correctable defects in technic or treatment. It seems essential, therefore, to describe not only the delayed deaths and the apparent and definite cures, but the early fatal results. It is presumptuous to record a patient as cured, as many hospital records show, if the patient leaves the hospital in apparently good condition. The reports in medical journals should detail at least the principal complications leading to death and make a distinction between those directly caused by or following the operation and those not related to the operation. Some of the former have been listed herein. The 17 deaths from shock in this series

occurred the day of operation, and at least some might have been foreseen and prevented. The cases of postoperative pneumonia developed up to the fifth day; the early ones were doubtless inspirational and unavoidable, but the late ones may have resulted from chilling. A recent English book on cancer of the rectum courageously admitted an operative mortality of 16.5 per cent and declared that one half of this percentage was due to sepsis. Eleven in this series of 106 cases of rectal cancers from Pennsylvania were fatal within twenty-four hours and 35 within a week; in not one was sepsis a factor, unless the two cases of peritonitis may be so regarded.

Finally, a survey has disclosed that many hospital records do not correspond with their death certificates; some show fewer, and others more, deaths than the state mortality records disclose. Death certificates also are notoriously incomplete and inaccurate. In the state in which this article is written, certified copies of over one half of the death certificates of adults are used as legal evidence. If all surgeons and hospital interns realized the importance of these certificates, they might be more particular in having the records reliable. Many antiquated forms of death certificates, printed and distributed years ago, are still being used. Every death certificate should give definite information as to whether or not an operation, and also an autopsy, was performed. If at any time there had been an operation for the particular disease causing or relating to death, the name of the operation and date should be recorded. No omissions concerning these questions should be allowed. From the carcinomas considered in this report there was a total of 4,696 deaths, and on only 1,061 certificates was the complete statement made that an operation had been performed on the definite date given, with the exception of a few cases in which two operations had been performed for the same disease.

SUGGESTED NEEDS

Operative mortality is an ambiguous term which needs a time limitation.

Death quickly follows operations because of a complication caused by, or directly related to, the operation, because another previous organic condition could not withstand the overload of the operation, or because the disease was an unrecognized, inoperable condition.

The fatal complicating conditions induced by the operation indicate for their prevention a need of greater improvement in surgical or nursing technic.

Operations done in the presence of numerous organic degenerations or conditions are a lottery, but are not necessarily contraindicated, as there is always hope. These complicating conditions should receive clinical, laboratory, roentgen and therapuetic attention.

By improved methods of examination, inoperable conditions are being recognized more and more without the performance of an operation.

More study of the actual causes of death is needed, and more ways should be devised to avert them. In reporting operative mortality, it is desirable that the physician should state the definite causes of death.

Reports of mortality should be standardized or defined to cover a certain period of time and to include or exclude certain described diseases, complications or conditions in order that other surgeons may draw parallelisms with their own experiences for the mutual benefit of mankind.

Death records constitute important statistical and legal evidence, and should be accurate and complete, stating all the facts.

ACUTE SURGICAL CONDITIONS WITHIN THE ABDOMEN OCCURRING DURING INFANCY AND CHILDHOOD

A STUDY OF THREE HUNDRED AND NINETEEN CASES *

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The acute surgical conditions within the abdomen that occur during infancy and childhood must be looked on as extremely important when one considers the high mortality rate in cases in which the condition is incorrectly diagnosed, treatment by surgical measures delayed or the patient allowed to go untreated. Nausea, vomiting of food or bile-stained mucus, crying on account of abdominal pain, visible peristalsis, abdominal rigidity, increased abdominal tension, an abdominal mass, decrease or absence of fecal stool, passing of bloody mucus from the bowel or fever and leukocytosis should attract one's attention to the abdomen instantly, and an investigation should be made to determine whether or not an acute surgical condition exists within the abdomen. The responsibility of recognizing such a condition rests with the family physician or the pediatrician who observes the sick child. The responsibility of promptly treating the patient lies with the surgeon called in consultation. Because the acute surgical conditions within the abdomen quickly cause nutritive disturbances, toxemia and death, the surgical consultant must be called early. It is deplorable to see a child with an intestinal obstruction of three or four days' duration, or with some similarly acute condition, brought into the hospital at the point of death, and to see the parents still hopeful that the child may be saved.

This study shows by statistical report the high mortality rate during childhood in cases of acute surgical conditions within the abdomen, and mentions some of the most frequent of these conditions. It is based on a review of 314 cases in children, from infancy to the age of 12 years, who were admitted to the Children's Hospital from January, 1924, to December, 1928. A few cases observed in private practice have been included, making a total of 319 in the series. We have observed the following conditions: acute appendicitis, intestinal obstruction, intussusception, peritonitis, abdominal tuberculosis, hypertrophic pyloric stenosis, congenital malformations such as occlusion of the duodenum

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and of the bile ducts, failure of rotation of the colon and Meckel's diverticulum, abdominal tumors, abdominal injury and foreign bodies. Certain conditions, such as gastric hemorrhage, gastric ulcer, abscess of the liver, cholecystitis, perforation or hemorrhage from typhoid or paratyphoid fever and intestinal obstruction from parasites, were not observed.

ACUTE APPENDICITIS

Acute appendicitis is the most common of the acute inflammatory conditions within the abdomen. The death rate from this condition is much too high. In the group of 236 patients operated on, there is a mortality rate of 8.4 per cent. The delay of the parents in calling a

TABLE 1.—*An Analysis of 236 Cases of Acute Appendicitis*

In Relation to Operative Observations and Mortality Rate

	Number of Cases	Percentage of Total	Deaths	Mortality Rate, per Cent
Acute appendicitis	122	51.0	0	....
Acute with gangrene	11	4.6	1	9.0
Gangrenous with rupture	75	31.7	14	18.6
Ruptured with abscess	28	11.6	5	17.8

In Relation to Sex and Color

	Sex		Color	
	Male	Female	White	Colored
Cases	136	100	185	51
Deaths	12	8	13	7
Percentage mortality	9.4	9.8	8	15

In Relation to Age and Mortality

Age, Years	Cases	Deaths	Mortality Rate, per Cent
1	4	1	25.0
2	8	0	....
3	19	4	21.0
4	9	1	11.0
5	21	5	23.8
6	24	3	12.5
7	25	0	....
8	29	2	6.8
9	28	1	3.6
10	30	1	3.3
11	25	1	4.0
12	14	1	7.1

physician or the delay of the physician in sending the patient to the hospital for surgical treatment was the cause of death in every instance. There was not a single death among the patients with acute appendicitis in whom diagnosis was made early and from whom the appendix was removed before gangrene set in. However, 114 patients, almost 50 per cent of the entire number, had gangrenous appendicitis, with or without rupture and with or without abscess, when admitted to the hospital. All the deaths occurred in this subgroup, which gives it a mortality rate of 17.5 per cent and makes the mortality rate in the group with appendicitis 8.4 per cent. Five patients in this subgroup were in such a serious condition when admitted to the hospital that they died within fourteen hours

after admission. If these five were eliminated, the mortality rate for the remaining cases would be 6.3 per cent. Many of the patients who died had been under the observation and treatment of physicians for several days. In some instances, in spite of repeated warnings to the contrary, the physician ordered castor oil or magnesium sulphate given to a child suffering from abdominal pain, nausea and vomiting; in other instances, ice bags were ordered applied to the abdomen, and the parents were led to believe that the disease could be "freezed out." On recognizing the possibility that a child has an acute abdominal condition, a physician should call a surgeon immediately. Laxatives and purgatives should not be given. The surgical treatment for appendicitis is laparotomy through a small muscle-splitting incision over the appendix;

TABLE 2.—*An Analysis of Seventeen Cases of Intestinal Obstruction*

	Sex		Color		Age			Operation				
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12, Inclusive	Relieving Obstruction	Relieving Obstruction with Resection	Relieving Obstruction with Colostomy	Relieving Obstruction with Enterostomy	Exploratory Laparotomy Only
Cases.....	10	7	14	3	9	5	3	4	3	1	7	2
Deaths....	5	3	7	1	4	4	0	3	0	0	5	0
Percentage mortality	50	42	50	33	44	80	0	75	0	0	71	0

Causes of Intestinal Obstructions

Operative Diagnosis	Cases	Deaths	Mortality Rate, per Cent
Adynamic ileum	1	0	0
Abscess of abdominal wall	1	0	0
Adhesions involving omentum	1	0	0
Band obstructing bowel	1	1	100
Coil of intestine attached to root of mesentery	1	1	100
Hirschsprung's disease	3	0	0
Intra-abdominal hernia	1	0	0
Meckel's diverticulum	1	1	100
Postoperative intestinal obstruction (appendectomy)*	5	4	80
Volvulus	2	1	50

* Also included among cases of acute appendicitis, but not included among cases of intestinal obstruction in table 8.

appendectomy and closure of the wound if the appendix is not ruptured; appendectomy and drainage if the appendix is ruptured. An appendical abscess should be opened and free drainage established. Whether or not the appendix should be removed in the case of an appendical abscess depends on the conditions found (table 1).

INTESTINAL OBSTRUCTION

Intestinal obstruction from stenosis, volvulus, peritoneal bands, tumors, inflammatory processes, and the like, is attended by an appalling mortality. In our group of cases of all varieties of intestinal obstruction, including intussusception, we show a mortality rate of 40 per cent, which is unquestionably too high and is more than likely due to

a failure to recognize the condition before the child has become too ill to stand an operation. Vomiting, abdominal distention, failure to expel gas or to pass fecal stools, dehydration and toxemia follow in rapid succession and lead to an early diagnosis if the signs and symptoms are carefully observed. An untreated patient with complete obstruction of the bowel will die. The surgical treatment consists in the subcutaneous or intravenous injection of physiologic solution of sodium chloride, laparotomy for the relief of the obstruction and enterostomy when indicated. Resection of the bowel may be necessary if gangrene is present. Eight of the seventeen children on whom operations were performed to relieve intestinal obstruction died, a mortality rate of 47 per cent (table 2).

INTUSSUSCEPTION

Intussusception occurs most often in infants, although it may occur in an older child. Its onset is characterized by sudden abdominal pain, usually in an apparently well child. The pain is accompanied by vomit-

TABLE 3.—*An Analysis of Thirteen Cases of Intussusception*

	Sex		Color		Age			Operation			
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive	Reduction	Resection with Anastomosis	Enterostomy	Exploratory Laparotomy Only*
Cases	11	2	10	3	12	1	0	9	2	1	1
Deaths	4	0	2	2	4	0	0	1	1	1	1
Percentage mortality	35	0	20	66	33	0	0	11	50	100	100

* Patient was moribund; nothing could be done.

ing and small stools, and later there is a failure to pass fecal stools. Blood-stained mucus may be passed from the bowel, or bloody mucus may be seen in the return from an enema. A tumor mass may be palpated in the right lower quadrant, or lying across the midportion of the abdomen. Later, abdominal distention, dehydration and toxemia may be observed. Surgical treatment is employed following subcutaneous or intravenous injection of physiologic solution of sodium chloride, and consists of laparotomy for the reduction of the intussusception, and resection of the bowel with anastomosis if the intussusception is irreducible or gangrenous. Among the thirteen patients operated on for the reduction of the intussusception, there were four deaths, a mortality rate of 30.7 per cent (table 3).

PERITONITIS

Peritonitis occurs most often as a secondary condition to an acute perforation, intestinal obstruction, intussusception, appendicitis, trauma, etc., and as a postoperative complication after laparotomy. As a pri-

mary condition, it occurs occasionally as an infection from the blood stream or lymphatics. The surgical treatment for secondary peritonitis is preventive, and treatment for the condition that may cause it should be undertaken as early as possible. Patients with primary peritonitis are not treated surgically unless an accumulation of pus can be located. When pus is found, it is drained by a simple procedure in the most direct way. Intravenous and subcutaneous injections of physiologic solution of sodium chloride and dextrose, transfusion of blood, gastric lavage and enemas are employed to maintain the body fluids at a normal level and to prevent toxemia.

HYPERTROPHIC PYLORIC STENOSIS

Hypertrophic pyloric stenosis is observed most frequently in infants during the early weeks of life. When the symptoms begin the child nurses well, but all milk and water are vomited after one or two feedings. The vomiting is projectile. Very soon after the onset of symptoms there is a noticeable loss in weight, the stools get smaller and

TABLE 4.—*An Analysis of Thirty-Two Cases of Hypertrophic Pyloric Stenosis*

	Sex		Color		Age			Operation: Pyloroplasty
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive	
Cases	25	7	25	7	32	0	0	32
Deaths	4	3	4	3	7	0	0	7
Percentage mortality	16.0	42.8	16.0	42.8	21.8	0	0	21.8

fewer and the vomiting continues. The upper part of the abdomen appears distended, and peristaltic waves of the stomach can often be seen passing across it. A tumor mass can often be palpated in the upper part of the abdomen to the right of the midline. Surgical treatment consists of gastric lavage, subcutaneous or intravenous injections of physiologic solution of sodium chloride, or transfusion of blood, followed by a laparotomy for the incision of the pylorus by the method of Fredet-Rammstedt. There were seven deaths among thirty-two patients with surgical conditions of pyloric stenosis, giving a mortality rate of 21.8 per cent. We believe that the mortality rate for hypertrophic pyloric stenosis could be reduced if the patients were referred earlier to the surgeon for operation (table 4).

CONGENITAL ABNORMALITIES

Congenital abnormalities, such as hour-glass contraction of the stomach and occlusion of the duodenum or lower part of the bowel, will produce symptoms during the first days of an infant's life. The surgical removal of the occlusion of the lumen and the reestablishment of its continuity are always done under most unfavorable conditions.

Nevertheless, an occasional patient survives, and the effort to save the infant should certainly be made. We should like to record one case of occlusion of the first portion of the duodenum, which occurred in an infant a few days old, and on whom operation was performed in another hospital. The constriction was excised and an anastomosis made over a catheter. The infant died within six hours after the operation, but at autopsy it was demonstrated that the occlusion had been removed and the continuity of the bowel had been reestablished. The child might have been saved had the operation been done a day or two earlier.

Failure of rotation of the colon favors the formation of volvulus, with a resulting intestinal obstruction. Volvulus from this abnormality

TABLE 5.—*An Analysis of Nine Cases of Congenital Abnormality*

	Sex		Color		Age		
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive
Cases	5	4	7	2	8	1	0
Deaths	4	3	5	2	7	0	0
Percentage mortality	80	75	71	100	87	0	0

Varieties of Congenital Abnormalities

Operative Diagnosis	Cases	Deaths	Percentage Mortality
Congenital occlusion of the bile ducts	2	2	100
Congenital occlusion of the duodenum	2	1	50
Esophageal obliteration	1	1	100
Failure of rotation of colon	2	2	100
Meckel's diverticulum*	1	1	100
Megacolon	1	0	0

Operations Performed	Cases	Deaths
Gastrostomy	1	1
Gastrostomy with cholecystostomy	1	0
Gastro-enterostomy	1	1
Enterostomy with abdominal drainage	1	1
Exploratory laparotomy only	2	2
Exploratory laparotomy, release of adhesions	1	0
Excision of occlusion of duodenum and anastomosis	1	1
Relieving of obstruction and removal of Meckel's diverticulum	1	1

* Also included among cases of intestinal obstruction, but not included among cases of congenital abnormality in table 8.

may occur at any time of life. We observed such a condition at autopsy in an infant who died from an intestinal obstruction. The child had been seen before death, but its condition was so serious that we considered an operation inadvisable. At autopsy we found the proximal half of the colon rotated only to the midline. There was a twisting on its mesentery of the proximal half of the colon, the cecum and a few feet of the small intestine. The surgical treatment for volvulus due to failure of rotation of the colon is laparotomy for the untwisting of the volvulus, and resection with anastomosis if the twisted segment of the bowel is gangrenous.

Congenital occlusion of the common bile duct prevents the bile from reaching the duodenum. The skin and sclera become yellow and later

almost bronze. The stools are clay-colored. The accumulation of bile and mucus above the point of obstruction will greatly increase the pressure within the duct. When the pressure in the obstructed duct becomes great enough to overcome the secretory pressure of the liver, marked damage to the liver takes place. Unless the bile duct or gall-bladder can be anastomosed to the duodenum or stomach, the infant will not live. Operation should be performed as early as possible after the condition is recognized.

Meckel's diverticulum does not cause symptoms if its tip is free and not inflamed. The tip, however, may be attached to the umbilicus by a cordlike remnant of the omphalomesenteric duct. A coil of intestine may become twisted about this cord; the lumen of the bowel may then become obstructed. The winding of the mesentery about the cord may cut off the arterial blood supply and the venous return, and as a

TABLE 6.—*An Analysis of Eight Cases of Abdominal Tumor*

	Sex		Color		Age			Operative Diagnosis			Operation		
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive	Sarcoma	Carcinoma	Hydronephrosis	Exploratory Laparotomy Only	Exploratory Laparotomy with Colostomy	Nephrectomy
Cases.....	5	3	8	0	5	2	1	6	1	1	6	1	1
Deaths.....	2	1	3	0	2	0	1	2	1	0	2	1	0
Percentage mortality..	40	33	37.5	0	40	0	100	33	100	0	33	100	0

result the twisted segment may become gangrenous. If an inflamed tip of a diverticulum becomes attached to the bowel or to the mesentery, a loop will be formed through which a coil of intestine may pass and become obstructed. When at operation a Meckel's diverticulum is found to be the cause of an intestinal obstruction, the tip must be made free. This will relieve the obstruction but it will not remove the cause. Therefore, the diverticulum must be removed. Its removal is usually accomplished by clamping the base, and cutting off the diverticulum. The stump is inverted by suture (table 5).

TUMORS

Abdominal and retroperitoneal tumors may cause obstruction of the bowel and require surgical intervention for relief. A benignant tumor may be removed, but a malignant one, such as a retroperitoneal sarcoma, is usually not removable. Only two cases of obstruction caused by

retroperitoneal tumor have been found in the series from the Children's Hospital. Elsewhere, we observed the case of a boy, aged 7, who had a partial obstruction of the colon caused by a large hydronephrosis which pressed on the splenic flexure (table 6).

ABDOMINAL TUBERCULOSIS

Treatment for abdominal tuberculosis is rarely surgical. In adhesive tuberculous peritonitis an obstruction may occur that would require surgical treatment. In this series, there are six cases of adhesive tuberculous peritonitis which required operation for relief from intestinal obstruction. In four cases enterostomy alone was sufficient; in two cases, however, it was necessary also to remove a collection of tuberculous pus from the peritoneum. The mortality rate was 33.3 per cent (table 7).

TABLE 7.—*An Analysis of Six Cases of Tuberculous Peritonitis*

	Sex		Color		Age			Operation	
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive	Enterostomy	Enterostomy with Drainage
Cases	5	1	4	2	1	3	2	4	2
Deaths	1	1	1	1	1	1	0	2	0
Percentage mortality	20	100	25	50	100	33	0	50	0

ABDOMINAL INJURIES

Abdominal injuries, such as falls or blows, may produce rupture of the liver, spleen, intestines, kidney or bladder. The occurrence of any one of these conditions may require surgical treatment. We had one patient, a schoolgirl, aged 8, who on being struck in the abdomen by a rock had a rupture of the middle colic artery with profuse abdominal hemorrhage. Laparotomy to tie off the bleeding vessels stopped the hemorrhage and saved the child's life.

FOREIGN BODIES

Most of the foreign bodies that reach the stomach pass through the bowel and are expelled from the rectum. If a sharp or pointed body perforates or becomes lodged in the bowel, or if an intestinal obstruction is caused, a laparotomy for the relief of the condition becomes necessary. In this study, we found two cases in which a safety-pin became lodged at the pylorus and would not pass. In each case it was necessary to perform a gastrotomy for the removal of the foreign body. Both patients recovered.

CONCLUSIONS

In the Children's Hospital, Washington, D. C., a large percentage of the children admitted for treatment are colored. In this series the cases in the colored children (21 per cent of the total number) undoubtedly raised the mortality rate as a whole. For instance, 56 per cent of the cases of acute appendicitis in the colored children were gangrenous with rupture or ruptured with abscess; there was no case of gangrene without rupture or abscess. Forty-five per cent of the cases in the white children were gangrenous, but the number with rupture or abscess was

TABLE 8.—*Analysis of 319 Cases of Acute Surgical Conditions Within the Abdomen*

In Relation to Sex, Color and Age

	Sex		Color		Age		
	Male	Female	White	Colored	Under 5	5 to 10	10 to 12 Inclusive
Cases	195	124	252	67	106	138	75
Deaths	30	17	31	16	29	14	4
Percentage mortality	15	13.7	12	23.8	27	10	5

In Relation to Operative Observations and Mortality

Condition	Number of Cases	Percentage of Total	Number of Deaths	Mortality Rate, per Cent
Acute appendicitis	236	73.9	20	8.4
Hypertrophic pyloric stenosis	32	10.0	7	21.8
Intussusception	13	4.0	4	30.7
Intestinal obstruction	12	3.7	4	33.3
Congenital abnormality	8	2.5	6	75.0
Abdominal tumor	8	2.5	3	37.5
Tuberculous peritonitis	6	1.8	2	33.3
Abdominal injury	2	0.6	1	50.0
Foreign body	2	0.6	0	0

relatively smaller (39 per cent). The mortality rate for this group of cases of gangrene with rupture and rupture with abscess was 25 per cent in the colored and 16 per cent in the white children. Four of the five patients who died within fourteen hours after being admitted to the hospital were colored; all four died within seven hours after admission. In three cases of intussusception in colored children there were two deaths, while among the white children there were only two deaths in ten cases, a mortality rate of 66 and 20 per cent, respectively. A similar difference was found in all the other groups except one. This greater mortality rate is, without doubt, caused on the one hand by the delay among the colored people in bringing the child's condition to the attention of a physician for diagnosis and on the other hand by the delay of the physician in making a correct diagnosis (table 8).

This study, like similar ones, has again brought out the fact that with children there is a very high mortality rate from acute surgical conditions within the abdomen, and that the earlier the condition is relieved by operation the better is the chance of saving the child's life.

Obviously, the utmost precautions must be taken to make an early and correct diagnosis of every acute condition within the abdomen, for should a surgical condition exist, the child's life is invariably at stake.

ULCERS DUE TO VARICOSE VEINS AND LYMPHATIC BLOCKAGE

A NEW PRINCIPLE IN TREATMENT *

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Before attempting to describe my conception of the principles underlying successful treatment in cases of ulcers due to varicose veins and lymphatic blockage, it is imperative to define more specifically the exact condition to be considered. Perhaps this can be done best by briefly mentioning the diseases to which I do not refer. It is not the small ulcer frequently found associated with varicose veins that has existed for only a short time, though such ulcers usually require more extensive operations than those commonly employed. It is certainly not the "trophic" ulcer, though sometimes, in these cases, a differential diagnosis is difficult and uncertain. It is not the syphilitic ulcer, although it is well to remember that patients with "leg ulcers" can have positive reactions to the Wassermann and Kahn tests and yet the ulcers apparently not be connected with syphilis. In such cases, of course, no operation should be done until after syphilitic treatment has been completed.

The type of ulcer to which I do refer is that one which all physicians remember dressing from month to month and often from year to year, without any marked success in the healing or diminution in the odor. Most of the modifications of Unna's pastes and adhesive straps have been used; some of the varicose veins have been removed with an insufficient amount of tissue under and around the ulcer; but, in spite of cherishing the hopes of an ultimate cure, most of these patients have returned only slightly, if at all, improved.

This state of affairs is best illustrated by the fact that in the twenty-seven cases on which this report is largely based, only two patients have not had previous operations. One patient in the series had nineteen operations, including all different kinds of skin grafts.

About twenty years ago, one fact became clear to me concerning this class of patients; namely, that the visiting surgeons, the resident surgeon, and often the interns did not want to be "bothered" with these disagreeable dressings, and, therefore, that the patients were not receiving the best possible consideration from the men in whom rested their best hope of relief.

In August, 1917, one of these unfortunate patients, who had had three separate and unsuccessful operations performed by surgeons in

* Submitted for publication, Jan. 5, 1929.

various parts of America, came to me insisting on an amputation for relief from the pain and the odor. After much persuasion and following some then unjustified promises, she consented to allow me to try the principle, which I believe is essential to successful treatment in this condition. As the patient has remained well for eleven years, and there has been but one failure in the other twenty-six cases, the presentation of this subject would appear justifiable.

In this case, in which the operation was not successful, I was able to heal the ulcer and greatly improve the edema of the patient's leg, but, unfortunately, an epithelioma developed at the site of the skin grafts (pinch grafts). Since the patient would not allow radium to be used, he drifted out of my observation, and died. I was unable to find out the cause of his death, but was informed that the malignant condition had become extensive a few months before death. Sections of this epithelioma were definite, and I believe that the "sore" on his leg, after the patient was no longer under my observation, was a continuation of the malignant condition and not a recurrence of the ulcer. Of this, however, I am not certain. As this case is in the series, it should be included here, in spite of any views that I might have concerning the etiology of the epithelioma in the graft.

By "success" I do not mean to imply that the leg has become normal or that it is as good as the opposite and unaffected leg. However, these patients have been relieved from pain; the ulcers have completely healed; the swelling of the leg has been greatly reduced, and they have returned to their various occupations, without any marked degree of physical discomfort or the necessity of wearing an elastic stocking or applying Unna's paste legging.

These cases of ulcers have many points that are fairly constant. In most of the patients the varicose veins have been removed; all of them have swelling of the feet and legs below and around the ulcer. All the ulcers "weep" a thin serous, odiferous, pale yellow fluid, which irritates the surrounding skin and sometimes nauseates the attending physician.

The ulcers usually start on the inner and lower side of the leg, frequently spread until they become the well known "saddle shaped" and, occasionally, encircle the leg. Associated with these ulcers are always edema and swelling, which are naturally more marked after prolonged dependent positions.

It is, perhaps, trite and certainly always puerile to call attention to the necessity of thoroughly considering the causes of a disease before contemplating the principles underlying its cure. However, with these ulcers, I am sure there has not been sufficient consideration given to the etiology, otherwise, the usual accorded treatment would have been different. The generally accepted view, of course, is that the whole

process is due to damaged varicose veins with subsequent trauma and infection. Until recently no consideration has been given to the lymphatic system, either as a causative factor or as to its value in applying curative measures. It is in a proper valuation of the rôle played by the lymphatic system, I believe, that a distinct advance in the care of these chronic ulcers is to be found. However, before further considering the association of the lymphatics with the failure to cure such a large percentage of the chronic ulcers, by commonly accepted surgical procedures, it would be well to review briefly all the tissues involved.

ETIOLOGY OF ULCERS

Varicose Veins.—Homans, in 1916 [1] and again in 1917,[2] presented the subject of varicose veins and ulcers in a most lucid manner and, to those who are interested in this subject, a careful perusal of both of his articles will be helpful in bringing every one to look at this complex problem from somewhat the same angle. He classified varicose veins according to their etiology into two groups: (1) those following mechanical forces due to occupations which require tension on the abdominal muscles, or prolonged standing on the feet, without exercise to assist in the return flow of venous blood up the leg by the muscles helping the veins push the blood from one valve to the one higher; (2) those due to infection such as phlebitis, "milk leg," etc.

A clear differentiation should be made between these two groups, for, with the cases of varicose veins following phlebitis, more careful attention should be paid to preventing the infection from involving the lymphatics. Infection is sooner or later superimposed on varicose veins due to mechanical causes, but the lymphatics are necessarily invaded by infection earlier when there is a primary phlebitis present.

It is possible that the day is not far distant when surgeons will be exercising segments of inflamed veins in postoperative and typhoid phlebitis, or "milk leg" following labor, etc. Such practice would hasten the period of convalescence, and also prevent infection from involving the lymphatics, which, as a rule, follows the course of the veins. Such practice would also tend to prevent the formation of future ulcers. For a "working basis," Homans also divided varicose veins into two other groups: (1) the simple surface varix, and (2) the surface varix complicated by varicosity of the perforating veins.

In order to differentiate properly these two classes, certain tests have been formulated, and it might not be out of place to recall them briefly. Not only do these tests help one in classifying the types of

1. Homans, J.: Surgery of Varicose Veins and Ulcers, Surg. Gynec. Obst. **22**:143 (Feb.) 1916.

2. Homans, J.: The Etiology and Treatment of Varicose Ulcers of the Leg, Surg. Gynec. Obst. **24**:300 (March) 1917.

varicose veins, but they also make one certain that varicose veins exist and that one is not dealing with a dilated and prominent vein associated with a diabetic, "trophic" or syphilitic ulcer. It is possible, though rare, to find calcification of the walls of varicose veins in patients who do not have arteriosclerosis. This process is probably a result of nature's attempt to prevent rupture of the wall of the vessel.

Tests for Classifying Veins: The three tests are as follows:

1. Trendelenburg's test is simple to apply. Have the patient lie on his back, raise the leg higher than the heart, then suddenly lower the leg below the level of the heart. The veins will fill out rapidly. If the walls of the veins are thickened, the impulse of the column of blood, unimpeded by the impaired valves, can be felt.

2. The "constriction" test is employed to ascertain whether or not the valves in the intercommunicating or "perforating" veins are functioning correctly. In this test, the leg is raised high enough to allow all the blood to run out and the walls of the veins to collapse. At this juncture, a constriction bandage (I have found the bandage of a blood pressure apparatus most useful) is placed around the thigh just tight enough to prevent the return of the blood through the surface veins. If the valves in the "perforating" veins are working, these prevent the blood from filling up the surface veins except in the normal manner. Such a process requires about one minute. On the other hand, if the valves in the "perforating" veins are not working properly, then the surface veins fill in from ten to thirty seconds, depending on how many of the valves in the "perforating" veins are not functioning.

3. The last test is one employed to demonstrate the patency of the deep femoral vein. The leg is allowed to hang down until the veins are distended, the constricting bandage is applied just tight enough to block the blood from going toward the heart through the surface veins. At this point, the leg is quickly lifted, and if the veins are collapsed in less than thirty seconds, then the patency of the deep veins is assured. Theoretically, this test sounds important, for were the deep veins completely obstructed and the superficial veins removed, gangrene might develop as a result of a blockage of the venous return. However, apparently a complete blockage of the deep veins does not occur, and I am unable to find in the literature any mention of such a surgical catastrophe. If there is ever a complete blockage of the femoral vein, it is more than likely that the rapid formation of a collateral venous system would prevent gangrene.

In many cases associated with edema and in abnormally fat people, these tests are of little value, for the veins cannot be seen and often cannot be felt. It is in such cases that a careful history, properly interpreted, is of paramount value in deciding on the best operative procedure.

Methods of Treatment: Varicose veins should be cured early and before secondary changes, such as infection, ulcers, lymphangitis, etc., have developed. At the start the condition can be corrected fairly easily by proper surgical measures. It is, in these cases that the comprehensive contribution of Dr. Homans has been of such great value. He called attention to the importance of correctly understanding the structure and function of the "perforating" veins which connect the superficial veins with the deep veins. It should be recalled that the valves in these "perforating" veins are so arranged as to allow the blood to go only from the superficial veins toward the deep veins. If these valves cease to function, there will naturally be a leakage of venous blood back into the soft tissues, with the consequent formation of a "stasis" ulcer, or the development of a varix. In accepting this state of affairs to be a fact, one must see the apparent necessity for ligating the "perforating" veins. Particularly is this true if the "constriction" test has demonstrated the valves in these veins to be defective.

Treatment for varicose veins by injection of various solutions has no appeal to my surgical instincts, for I cannot rid my mind of the fear of washing off emboli from some possible thrombus, in spite of the fact that the literature does not report such occurrences. It has been suggested to tie off the saphenous vein just before it enters the femoral vein and then to inject, and, in this way, to lessen the aforementioned possibility. If one is going to resort to surgical measures, one should employ surgical principles and not combine operation with "blind" procedures.

Unquestionably, many patients with varicose veins have been cured by the injection methods, but this procedure is not without its dangers. While no cases of death from emboli have been reported, still the literature contains the report of deaths from an apparently latent infection, which has been "stirred up" by the intravenous and perivenous infections. Most advocates of the injection methods warn against the possibility of injecting the solutions into the tissues around the veins on account of the subsequent formation of abscesses, etc., from tissue necrosis. Therefore, the method is not as easy as it might at first appear to be. In most of these large ulcers, it is impossible (due largely to the great amount of swelling present) either to see or to feel the veins. In such cases no injections should be attempted. I have seen four cases of ulcers of the leg in which the injection method had been employed: one of the patients did not have the ulcer until after injection into the vein, and there had been no improvement in the condition of the ulcer in the other three. However, I have seen personally many patients with varicose veins who have been either cured or markedly benefited by the injection method. When the varicose veins are definitely due to mechanical causes, intravenous injections might be a valuable addition

to the treatment; but when they are due to infection, the principle is unsound surgically and hazardous from a practical point of view. It is also next to impossible to estimate whether a latent infection in the vein is present or not.

As will be shown later in this article, the obstruction of the lymph channels plays an important rôle in the causation of ulcers, and the chemical irritation, with subsequent fibrosis on which the success of the injection method depends, serves to increase the chances of a lymphatic blockage, and, thereby, tends, possibly, to produce future ulcers. I have had no first hand experience with the method, but have seen a few patients treated elsewhere. I am not impressed with the advisability of forsaking sound surgical principles and substituting a method having theoretically an immediate danger of emboli as well as causing an almost certain injury to the lymphatic drainage with the future development of an ulcer.

No one operation is applicable to all types of varicose veins, but there is one procedure, which should never be omitted in any case, and, that is, the tying off, first, of the saphenous vein close to its entrance to the femoral. If possible, the vein should be removed from the thigh to a point below the knee. It is best to do this first before any form of attack is made on the veins in the leg. Numerous operations have been reported, such as: the ligation operations of Trendelenburg [3] and Schede,[4] the wide dissections of Madelung,[5] the spiral incision of Rindfleisch [6] and the "stripping" operation of Mayo [7] with many modifications—sufficient, in fact, to demonstrate that no one operation has been satisfactory for all classes of cases. The one selected should be applicable to each particular case according to the distribution and character of the veins, as well as the general physical condition of the patient.

Arteries and Veins.—After having studied the veins, one's attention naturally turns to the valuation of the rôle taken by the arteries and nerves. These are considered together, largely because of the intimate relation existing between the arteries and the sympathetic nerves. Naturally, in this connection one turns to the pioneer work of René

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3. Trendelenburg: Ueber die Unterbindung der Vena saphena magna bei Unterschenkelvaricen, Beitr. z. klin. Chir., 1890, vol. 7.

4. Schede: Ueber die operative Behandlung der Unterseckenkelvaricen, Berl. klin. Wchnschr., 1877, vol. 14.

5. Madelung: Ueber die Anschaelung cirsoider Varicen an dem unteren Extremitaeten, Verhandl. d. deutsch. Gesellsch. f. Chir., 1884, vol. 13.

6. Rindfleisch: Arch. f. klin. Chir., 1908, vol. 86.

7. Mayo, C. H.: Treatment of Varicose Veins, Surg. Gynec. Obst. **2**: 385, 1906.

Leriché [8] and his co-workers. It is logical to presume that the infection, etc., which starts in the veins should ultimately involve the arteries, either by direct extension of the infection or by the increased resistance to the onward progress of the blood, causing a hypertrophy of the arterial wall. Evidently, Leriché [8] felt that by doing the periarterial sympathectomy he was able to overcome whatever handicaps might have been placed on the arteries by the formation of connective tissue around these ulcers. In fact, he stated:

> The ulcer is consecutive to a dermo-epidermic necrosis springing from an arterial ischaemia, sometimes spasmodic, which creates a positive loss of substance always much greater than the apparent ulceration. The ulcer is incurable because the bad local circulatory conditions lead to an imperfect nutrition of the soft parts where the viability of the tissues is always mediocre.

In November, 1916, Leriché with his associate R. Fontaine [9] reported results in sterilization of infected wounds and ulcers by periarterial sympathectomy. Briefly, they stated three observations:

1. A chronic ulceration "is always infected to infinity by a large variety of microbian species." As the bacteria are found deep in the tissues, external medication is of no avail.

2. Soon after sympathectomy, the appearance of the ulcer changes.

3. From the fifth to the thirteenth day the wound is "practically and bacteriologically sterile." They ascribed this sterilization of the wound to the "afflux of leucocytes to the level of the ulcer." After making the ulcer sterile, they believe in replacing the lost skin by means of grafts, and prefer the Davis graft. They found that this sterilization of the ulcer is of comparatively short duration, it is, therefore, necessary to place the graft on the surface before reinfection takes place. They found the most favorable moment to be between the seventh and twelfth day after periarterial sympathectomy. Leriché, in speaking of varicose ulcers, made this final statement: "I make it a habit at the time of the sympathectomy to add to it a saphenectomy after the manner of Babcock." This is but another illustration of how, when one becomes enthusiastic concerning some particular point, one is apt to attach to it undue importance.

Knowing these views of Leriché, I decided to try periarterial sympathectomies in preparation for radical operation in two of these cases of extensive varicose ulcers. I regret that my results were not conclusive, for I could not see any more change in the ulcers on which

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8. Leriché, René: Surgery of the Sympathetic System, Ann. Surg. **88**:449, 1928.

9. Leriché, R., and Fontaine, R.: The Sterilization of Infected Wounds and Chronic Ulcerations by Periarterial Sympathectomy, Ann. Surg. **84**:625 (Nov.) 1926.

I had done a periarterial sympathectomy than I thought I had observed in somewhat similar cases of ulcers in which treatment consisted of rest and elevation of the leg. In these two patients, I did not obtain sterilization of the wound. With rest and elevation of the leg, there is lessened subcutaneous venous stasis and as a result decreased bacterial invasion. In these two patients, the prompt cessation of pain within twenty-four hours after the periarterial sympathectomies was striking. There was far more and quicker relief than is usually seen following rest and other methods employed in the preparation of patients for any operation for varicose ulcers. However, two cases are not sufficient material on which to make proper deductions, and, certainly, Leriché's reputation and surgical logic is such that his method deserves a much more extended observation by numerous surgeons.

It is possible that the combination of the lumbar sympathectomy or sacrosympathectomy with the periarterial sympathectomy might prove more satisfactory than the periarterial sympathectomy by itself. Such an operation is as extensive as the radical operation for varicose ulcer, which, when properly performed, gives definite and gratifying results.

Recently there have been numerous reports of the injection of alcohol into the nerves close to the ulcer for relief from pain. This, at best, is only a palliative measure and has no practical application in the preparation of the patient for operation, for pain is effectively relieved with rest and elevation of the leg. I cannot help but feel also that such injections produce fibrous tissue; thereby the lymphatic blockage is increased, and the treatment may prove distinctly harmful. However, physicians are just beginning to learn something about the surgical treatment of the nervous system and should withhold all hasty judgment.

It is interesting to recall that in 1851 Carnochan (quoted by Matas) ligated the main artery of the limb with the "view of restricting the circulation and, thereby, diminishing the tendency to lymph dropsy and stasis." No benefit resulted from this procedure.

It has been clearly demonstrated that the pigmentation of the skin seen before the ulcer forms is due to subcutaneous venous stagnation and the consequent failure of the venous and lymphatic systems to remove certain of the blood pigments. After the ulcer forms, the pigmentation usually continues to exist for several inches around the ulcer. With the skin in such a condition, the slightest trauma results in an abrasion on which infection is superimposed, and at such a site an ulcer quickly develops. The protective invasion of round cells is soon replaced by fibrous infiltration. Following this, blockage of the arterial supply, as well as of the venous and lymphatic return, occurs. If the infection is virulent, naturally necrosis of skin which sometimes involves extensive areas soon follows. To add discomfort, there is poured out on the skin a thin, watery, yellow fluid with a most disagreeable

odor. This excretion further irritates the already devitalized skin. It is more than likely that some of this excretion is lymph. To a less degree the same processes attack the subcutaneous fat, the fascia, the muscles, the periosteum, and, in severe cases, the tibia. In this series, there have been only two cases extensive enough to cause osteitis of the tibia. In both of these cases, there was the history of the "shedding" of superficial sequestrums. In fourteen other cases, not only was the periosteum involved, but there was also eburnation of the tibia to such an extent as to suggest strongly that the infection had extended to the bone.

With this extensive infection, the usual fibrous tissue replacement occurs, and, as years pass, this layer often becomes almost like leather. This layer of fibrous tissue sometimes contains areas of calcification. At this stage of the development, I believe two important factors are usually overlooked in the surgical treatment. The first is the one to which Dr. Homans has called attention, e.g., the "perforating" veins. The second is the lymphatics, which I shall now consider.

If the edema usually associated with these large ulcers and always present in the recurrent cases is due to a lymphatic blockage it is self-evident that measures must be instituted to overcome this condition, before any rational hope of a permanent cure can be entertained.

The Lymphatics.—Matas [10] called attention to the fact that simple mechanical edema is incapable of exciting proliferation of the connective tissue. He further stated that Unna, Darier, Le Dantec, Sir Patrick Manson and others have demonstrated that the blocking of the lymphatic channels with *Filariae* is not by itself sufficient to produce these connective tissue changes, but he thought that repeated attacks of streptococcal infection superimposed on the existing lymphatic block is necessary to cause the conditions found in the subcutaneous tissue and skin. A history of repeated attacks of "erysipelas" is associated with cases of "ulcer." While such attacks are not superimposed on a lymphatic blockage produced by *Filariae,* these streptococcal infections are grafted on a lymphatic blockage due to lymph coagulation and pressure from fibrous infiltration. Such being the situation, one occasionally sees an "elephantoid state" associated with these ulcers. Gesser, with Dr. Matas, reported one such case in 1913.

In his operation for elephantiasis, Kondoleon suggested a possible means of meeting this surgical dilemma.

Before accepting either the theory of the lymphatic block or Kondoleon's hypothesis of establishing communication between the superficial

10. Matas, Rudolph: The Surgical Treatment of Elephantiasis and Elephantoid States Dependent upon Obstruction of the Lymphatic and Venous Channels, Am. J. Trop. Dis., 1913, vol. 1.

and the deep lymphatics to relieve edema, it would be well to consider the accuracy of these theories.

In 1913, Florence Sabin [11] described the origin and development of the lymphatic system. To those interested in the embryology of this subject, a perusal of her articles will prove both profitable and interesting. Speaking in general terms, the lymphatics of the leg might be said to follow the veins in their development and distribution. As in the veins, there is a superficial and a deep system of lymphatics, but there is no intercommunication except through the popliteal and inguinal lymph nodes.

It has been demonstrated by Sabin, MacCallum, Lewis and others that the lymphatic supply is a distinct system of endothelial-walled vessels, not related either to the serous cavities or to the connective tissue spaces with which it has been confused so long, for the lymphatics grow by "budding" at the tips of their capillaries.

My own belief is that any accurate knowledge of the distribution of the lymphatics in the leg is limited and much confused at the present time, but with the constantly improving methods of injecting the various dyes there will soon be more reliable information.

Opie [12] has determined the coagulation time of lymph to vary between ten and twenty minutes as compared with that of blood, which is between four and six minutes. He expressed the belief that a slow coagulation of the lymph is due to the "scant quantity of thrombokinase present." This, taken in consideration with the fact that lymph contains no blood platelets, which is well known are essential to the formation of thrombi, would seem to prove that the blockage of the lymphatic channels from the coagulation of lymph is a rare occurrence. Opie,[12] however, has further proved that lymph coagulates readily within two and one-half minutes if "serum obtained from the surface of the wound" be added to the lymph. In his conclusion he stated: "The slow coagulation of lymph is hastened by the addition of thrombokinase, and thrombosis within lymphatic channels occurs when thrombokinase is liberated by the tissues in the wall of the lymphatic necrosis of cells in contact with the lymph stream favors thrombosis within the lymphatic vessels by bringing thrombokinase into contact with the circulating lymph." Certainly, if "necrosis of cells" and serum are prerequisite for the rapid coagulation of lymph, both are found in abundance in an ulcer. If this be true, it is reasonable to assume that blockage of lymphatic channels by rapid coagulation of lymph is as apt to occur with ulcers of the leg

11. Sabin, Florence R.: The Origin and Development of the Lymphatic System, Johns Hopkins Hosp. Rep., 1913.

12. Opie, Eugene: Thrombosis and Occlusion of Lymphatics, J. M. Research, 1913-1914, vol. 24.

as with veins when occluded by the formation of thrombi. Not only is there the possibility of lymphatic blockage from within its channel, but the certainty of obstruction from without, by the formation of the fibrous infiltration formed following infections. The deep lymphatics are largely protected from these changes by the protecting layer of fascia.

Kondoleon,[13] in 1912, in his operation for the cure of elephantiasis, advocated the removal of a long strip of this fascia so as to allow the lymph, etc., to be removed by the deep lymphatics. It is interesting to note that a review of the literature discloses only 142 cases of the Kondoleon operation for elephantiasis nostras streptogenes. In these reports, all of the patients have been improved. Kondoleon [14] reported twenty of these cases, and concluded that the ultimate outcome of the whole is not as good as was anticipated from the great improvement at first. All his patients have been improved, and in none did the condition grow worse. There must be a few hundred such operations which have not been reported in the literature, for I personally know of but few clinics where one or more of the Kondoleon operations have not been done. Burke [15] reported twelve cases but did not give the etiology of any of them. As these cases were in Porto Rico, *Filariae* might have been present. His results were bad. Sistrunk [16] stated that there has been improvement in his series of 100 cases, though in some instances, he had to do three or four operations before obtaining a satisfactory result. His experience has also been somewhat similar to that of Kondoleon as regards the permanency of the improvement. Sistrunk, further, feels that a large factor in the improvement of these patients is to be found in the removal of the diseased tissue, in addition to the removal of the fascial barrier and the regeneration of the lymphatics.

Naturally, the next question to arise is: What proof is there of any regeneration of the lymphatics? Of course, the success of the Kondoleon operation in improving the cases of elephantiasis nostra streptogenes is some clinical proof, but, in addition to such testimony, there has been much interesting experimental work to show conclusively that lymphatics do regenerate. The beneficial results following the removal of the fascia might be due to having the superficial tissues drained by the deep

13. Kondoleon, E.: Die operative Behandlung der elephantiastischen Oedema, Zentralbl. Chir., July 22, 1912, vol. 39 (six cases).

14. Kondoleon, E.: Arch. franco-belges de chir., Brussels **27**:104 (Feb.) 1924. (Now has twenty cases. The ultimate outcome on the whole is not as good as was anticipated from great improvement at first.)

15. Burke, Garry R.: Results in Porto Rico of Kondoleon Operation for Elephantiasis of Extremities, Surg. Gynec. Obst., December, 1928.

16. Sistrunk, Walter, personal communication to the author, Dec. 12, 1928.

lymphatics. However, as one reviews the experiments of Halsted,[17] Coffin,[18] Evans,[19] Opie,[12] MacCallum,[20] Reichert,[21] Sabin [11] and others, one cannot help but be impressed with the possibility and also the rapidity with which collateral vessels form and lymphatic vessels regenerate.

In 1906, Coffin,[18] under the direction of MacCallum,[20] sewed a loop of intestine through the wound in the skin. He waited for about ten days for granulations to form, and then made injections into the normal lymphatics on the surface of the loop. Not only did these lymphatics fill, but the injected fluid penetrated a short distance into the granulation tissue. Serial sections of these granulations showed these "penetrations" to be newly formed lymph channels. Histologically, it was not difficult to differentiate these channels from blood vessels, but, to be sure no mistake was made, he injected other colors into the blood vessels. Microscopically, these sections showed "sprouts into the granulation tissue which resemble closely sprouting blood vessels." The lumen of the channel narrowed to a point where the injection stopped. Beyond this there was a continuation of the endothelial cells, and it is probable these were the forerunners of future lymphatic channels.

Coffin's conclusion is: "It is seen here as always that the lymphatic channels are perfectly sharply outlined independent structures completely formed of endothelial cells and standing in no more intimate relationship with the crevices of the connective tissue than do the capillary blood vessels."

Structurally, the lymphatic channels are so delicate that they are hard to recognize, but since the introduction of proper methods of injecting dyes into them, knowledge of their presence in various organs has greatly increased. Even as far back as 1908, Evans [19] demonstrated the formation of new lymphatics in a round cell sarcoma. These new lymphatics were found to be in direct connection with the preexisting lymphatics, and as early as 1863, Krause,[22] by making injections with colored fluid into the skin adjacent to tumors, demonstrated the continuation of true lymphatics into new growths. If new lymphatic channels can form in a new growth, it is reasonable to suppose that they

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17. Halsted, W. S.: Swelling of the Arm After Operations for Cancer of the Breast—Elephantiasis Chirurgica—Its Cause and Prevention, Bull. Johns Hopkins Hosp. **32**:309 (Oct.) 1921.

18. Coffin, T. Homer: On the Growth of Lymphatics in Granulation Tissue, Bull. Johns Hopkins Hosp., August, 1906, vol. 17.

19. Evans, H. M.: On the Occurrence of Newly-Formed Lymphatic Vessels in Malignant Growth, with a Demonstration of Their Origin and Ingrowth in the Metastases of a Round-Celled Sarcoma, Bull. Johns Hopkins Hosp., August, 1908, vol. 19.

20. MacCallum, W. G.: Bull. Johns Hopkins Hosp. **17**:277 (Aug.) 1906.

21. Reichert, F. L.: The Regeneration of the Lymphatics, Arch. Surg. **13**:871 (Dec.) 1926.

22. Krause, W.: Ueber Lymphgefässe im Geschwülsten, Deutsche Klin., 1863.

can develop in the normal tissue found below the fascia and, to a lesser degree, in the somewhat fibrosed structures between the skin and the fascia.

In 1926, however, Reichert [21] in a series of experiments on dogs clearly demonstrated the formation of new lymph channels through scar tissue. He also showed infection delayed which, if extensive, almost prevented the penetration of new lymph channels across the barrier of scar tissue. It is interesting to recall that Reichert, with the late Professor Halsted, was trying to find the cause of the swelling of the arm which sometimes follows extensive operations for carcinoma of the breast.

Reichert quoted Bilroth as having said, in 1863, that lymphatics did not grow across scar tissue in the early stages. He further quoted Billroth as follows:

> You see that the young cicatrix, on the seventh day, when it still consists almost exclusively of cells, has no lymphatic vessels; these cease immediately at the young cicatrix; they do not form in the cicatrix until the fibrillary connective tissue bundles form. The granulation tissue also has no lymphatic vessels; where the inflammatory new formation, where the primary cellular tissue forms, the lymph vessels are mostly closed, partly by fibrous coagulations, partly by new cell formations. These observations have also been confirmed quite recently by Losch of St. Petersburg by examination of the traumatically inflamed testicles.

Reichert, in his experiments on dogs, severed all structures in the leg down to and around the femoral artery and vein, even cutting around the periosteum, as well as removing the adventitia from the vessels. All tissue was reapproximated with silk sutures, and no infection resulted in his series of experiments. India ink was injected into that portion of the leg distal to the transverse section. It was found that lymphatics formed across the line of scar as early as in four days, if the structures were accurately approximated. The superficial lymphatics were the first to regenerate, but the deep channels were found crossing the scar as early as eight days. The edema of the leg reached its maximum about the second day and began to subside about the fourth day or just about the time when regeneration of the lymphatic and venous channels was developing across the scar. He further proved, by injecting granules of India ink into the lymph channels, thereby blocking them, that the edema reappeared in spite of the fact that the veins had been reestablished in the meantime. He even went so far as to demonstrate that ligating the femoral vein did not cause edema if ligation was done in these dogs "when the subsidence of the swelling has just been completed." He further extended his experiments to prove that the edema was due to lymphatic and not to venous blockage. Infection, in the region of the scar, greatly delayed the regeneration of lymphatics.

Eloesser,[23] experimenting on the ears of rabbits, found that the lymph channels ultimately form across a scar, extending down to the cartilage, but he estimated that it took about four months for them to regenerate. He also found inoculation with a strain of streptococci (produced in the laboratory of Dr. Gay at the University of California) delayed this regeneration even longer.

Matas,[24] in 1913, called attention to the fact that chronic edema and swelling caused by lymphatic blockage was not in itself sufficient to produce the fibromatosic changes found in elephantiasis, but that such changes were dependent on repeated infections probably with various strains of streptococci. It may be that the hard, browny swelling found associated with these ulcers is not an "elephantoid" process, but to one seeing these ulcers of many years' duration, the relationship is most suggestive. Certainly, the usual history of repeated infections ("erysipelas") has much to do with the condition of the skin and underlying tissues. Homans,[2] in referring to the recurrent swelling associated with one of his cases of ulcer, stated "The difficulty may quite possibly be with the lymphatics, and the condition may be one of elephantiasis."

Some years ago, believing that the streptococcus plays an important part in these ulcers, I made a few injections of the stock (polyvalent) vaccines without any appreciable results. I have not been successful in obtaining any cultures from the tissues remote to the ulcer with which to make an autogenous vaccine. Either in the ulcer, or close to the same, the bacterial flow is too abundant to make a satisfactory vaccine. It might be that by following the method of Burbank of New York, or by removing an inguinal gland and "grinding" up the same after the technic developed in Baer's department in the Johns Hopkins Hospital, it would be possible to obtain an autogenous vaccine that would be of value in preparing the leg for operation as well as of service in preventing reinfections after operations. I expect to try the method of Burbank on the next few patients and hope to have more definite information relative to Baer's technic so that I can employ this also. Such studies will be the basis of a later report.

"Milk Leg": Phlegmasia Alba Dolens.—The extensive "milk leg" which follows phlebitis of the femoral and iliac veins presents a more difficult surgical problem than do the varicose veins and ulcers which follow phlebitis of the great saphenous vein. Owing to the support given to the walls of the deep veins by the surrounding muscles and fascia, as well as the assistance rendered by muscular contraction, varicosity

23. Eloesser, Leo: Obstruction to the Lymph Channels by Scar, J. A. M. A. **81**:1867 (Dec. 1) 1923.

24. Matas, Rudolph: Surgical Treatment of Elephantiasis and "Elephantoid" States Dependent on Chronic Obstruction of the Lymphatic and Venous Channels, Am. J. Trop. Med., no. 1.

of deep veins must be limited, if it ever occurs. Phlebitis of the femoral and iliac veins is not uncommon and when it does occur, there usually follows the well known swelling of the leg and sometimes the thigh, which is often associated with numerous small ulcers. This is a different picture from that of the large ulcer usually found "riding" on one of the superficial veins following phlebitis of the great saphenous vein. Associated with phlebitis, a thrombus is frequently found. When this occurs in the superficial veins there usually follows a compensatory dilatation of the veins with stretching of their walls, a consequent leakage of the valves, with the formation of varicose veins. When the phlebitis, however, attacks the femoral or iliac veins, there is damming back of blood (owing to the decreased size of the lumen of the vein) on the superficial system with, sometimes, the formation of varicose veins of both the perforating and the superficial veins. More often, the leg and thigh become edematous, sometimes presenting small ulcers, and the dilated veins are not seen.

My belief is that the edema, etc., is due not only to the blockage of the venous system, but also to the obstruction of the return of lymph. The obstruction of the lymph is due to the blockage of the lymph channels and nodes by the fibrous tissue, which follows the infection. This class of cases is most difficult to handle and the solution is found not only in the attention given to the veins, but also to the lymphatics. In such cases I believe both the width and the length of the fascial strip removed should be greater than the amount of fascia removed, when the lymphatic block is confined to the superficial lymphatics. To establish a free path for the unhampered regeneration of the lymphatics, it is necessary to remove the strip of fascia higher than the edema, particularly is this true when the swelling is the result of involvement in the deep vessels and lymphatics. Of course, in these cases the strip of fascia is removed from both the inner and the outer sides. In one case in which the swelling extended well up on the thigh I obtained a gratifying result by removing, on the outer side, the fascial strip several inches above the crest of the ileum. The extent of fascia removed is dependent, as in the Kondoleon operation for elephantiasis, on the amount of swelling present.

Walther,[25] before the advent of the Kondoleon operation, implanted the ends of small rubber tubes under the fascia lata, and then the other ends terminated in the peritoneal cavity. He did this in eleven cases of elephantiasis, and obtained marked, but temporary, improvement in all cases. He further advocated that such tube drainage be tried in cases of extensive and high phlegmasia alba dolens where the signs indicated

25. Walther, C.: Bull. Acad. de méd., Paris **79**:195, 1918. (Buried Drainage for Elephantiasis. No. 10 nonpeforated rubber tube from under the fascia into the abdominal cavity; three cases, all successful.)

involvement of the iliac vessels. However, he did not report operating on a patient.

I do not mean to imply that the swelling usually associated with these extensive ulcers of long duration is an elephantiasis. However, I do state that if these ulcers are allowed to continue long enough, the surrounding tissue will assume an "elephantoid state," which clinically and histologically resembles elephantiasis nostra streptogenes. If this observation is correct, extensive removal of the fascia is indicated in such ulcers. In ulcers of not so long standing and of limited involvement, this principle should also be applied, but such a condition does not require as extensive removal of fascia. The fact that recurrences are frequent after removal of varicose veins and grafting the ulcers shows, to my mind, that sufficient lymphatic return has not been provided.

I readily admit that in my enthusiasm I have been led to apply the operation in a few cases in which less extensive measures would probably have sufficed. However, the principle of establishing a sufficient lymphatic return is, I am sure, correct.

METHOD OF OPERATION

Before any operative procedure is attempted on these ulcers, the patient should be in bed with the foot elevated until the edema has greatly subsided. Such a course will add to the ease of the operation and decrease the chances of stirring up an old latent infection. Sometimes it is necessary to wait for several weeks before operating, but, even in such an event, time is gained, because patients treated in this manner have a much shorter postoperative convalescence.

As a rule, most of these patients have already had the varicose veins removed; if not, the veins should receive the proper attention at the time the remainder of the operation is being done. There is no difficulty in doing this as the same incisions give proper exposure for any desired procedure. The extent of the operation depends on the amount of edema present, the duration of the trouble, the age of the patient and other factors. If the edema is limited to the leg, the fascial strips need not be removed in the thigh. The longer the duration of the ulcer and the more extensive the edema, the more imperative it is to remove larger strips of fascia. The operation advocated is not different from many others in that it should be modified to suit the case. The following is a description of the operation applicable to the most extensive cases.

Incisions are made through the skin on both the inner and the outer side of the thigh and the leg. If the ulcer is on the inner side of the leg, as it most frequently is, the inner incision is carried to, roughly, within 3 inches (7.62 cm.) of the ulcer. The fat is then undermined for about 2 inches (5.08 cm.) on each side, removing with it all possible varicose veins that might have been overlooked. It is important to ligate all "perforating" or intercommunicating veins. A strip of fascia about 2 or 3 inches wide is then removed, as is done in the Kondoleon operation. The sides from which the strip of fascia have been removed are sewed down to the muscle with interrupted sutures. The skin on the side opposite to the ulcer is now approximated with silk sutures. On the side of the leg on which the ulcer is located an estimate is made of the amount of skin required to cover the raw area

from which the ulcer will have been removed. This is done in order to make a "chain" tubal graft which will be transferred at the proper time. The method of making this chain graft is simpler to do than to describe.

Most of the fat either from the anterior or posterior edge of the incision is removed for a distance of about 2 inches (5.08 cm.). The posterior edge is usually on the inner side, the easier site, for this edge is more freely movable as it does not lay over the tibia. Two, three, four or five incisions (depending on the amount of skin required are made), each about 3 inches (7.62 cm.) long and about 2 inches (5.08 cm.) from and parallel to the original incision. The ends of these incisions should be about 1½ (3.81 cm.) to 2 inches (5.08 cm.) from each other, and the lower one should end about 3 inches from the edge of the ulcer. A series of 3 inch "tube" grafts are then made by rolling the edges together and sewing them accurately, with interrupted sutures, so as to leave as little scar as possible. After these short "tube" grafts are made, the skin is approximated by sewing the cut edges under the grafts, except at the points between the ends of the grafts. The spaces between the ends of the grafts form a series of pedicles, which are to be cut later. Even at the site of the pedicle, the graft is loosely shaped so

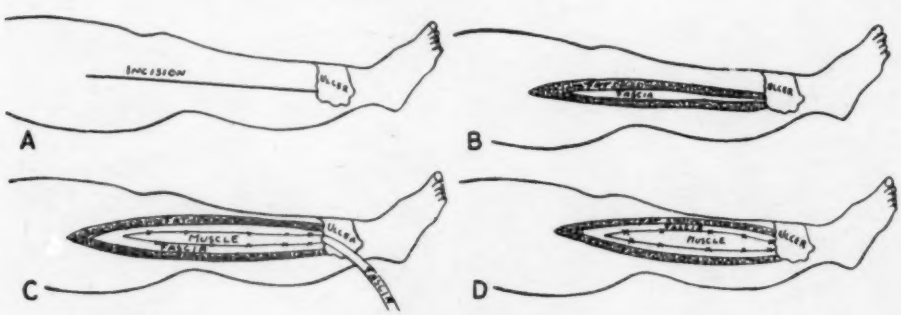

Fig. 1.—Stages in operation for ulcer of the leg: *A*, incision on the outer side of the thigh and leg; *B*, incision carried down to fascia (the same type of incision is made on inner side when the ulcer is extensive); *C*, strip of fascia partially removed and the cut edges of the remaining fascia sewed to the muscle; *D*, strip of fascia completely removed and the cut edges of the remaining fascia sewed to the muscle.

as to become part of the future long tube and is held in position by sutures placed tightly enough only to shape the graft.

It is perhaps needless to state that up to this time the ulcer has been carefully covered and the operative field protected from contamination. After the application of proper dressings, the ulcer is exposed and all fibrous tissue removed with the ulcer. I have found it advantageous to cover the ulcer with gauze and make the incision well away from the margin of the ulcer. The incision is carried down until normal tissue is found, and then the whole mass is removed by dissecting underneath the thick base. It is essential that all fibrous tissue be removed to prevent any future lymphatic block. Any "perforating" or intercommunicating veins found (and usually there are several present under the ulcer) are carefully ligated. The operative field is cleared again, draped with fresh towels, etc., gloves and gown changed and a clean set of instruments used. This is required because it is necessary to remove the fascia down to the raw surface at the site from which the ulcer has been dissected, and therefore an aseptic field is again essential.

Much, but apparently not enough, has been said about the necessity of removing tissue wide of the ulcer in every direction until somewhat healthy tissue is found. Over twenty years ago, while an assistant to Dr. J. M. T. Finney, I well recall his insistence on the wide removal of these ulcers, particularly as regards the "leather-like" base. This procedure, associated with the proper attention to the varicose veins, will cure a large percentage of these patients, but it will not relieve either the multiple ulcers or those of long duration with swollen, brawny skin. The reason for this is probably that a ring of fibromatosis is left around the site from which the ulcer has been removed. In such cases it is necessary to remove a strip of fascia with some diseased subcutaneous fat, etc., in order to secure free communication between the superficial and the deep lymphatics. On one's willingness to do this thoroughly often rests the success of the operation. It is usual to find that this wide dissection carries one down to the periosteum and sometimes through

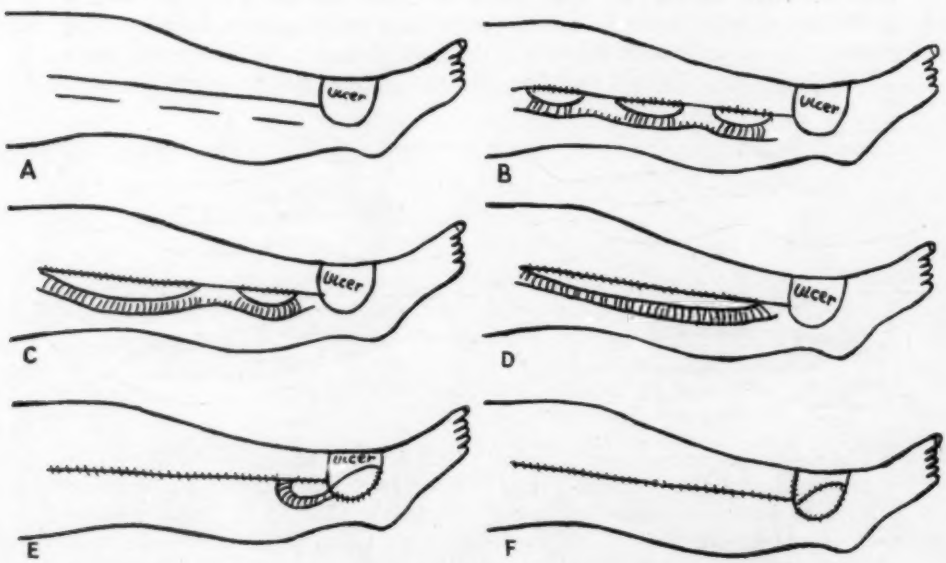

Fig. 2.—Further stages in operation: *A* shows three parallel incisions posterior to the first incision; *B*, skin approximated under these "tube" grafts; *C*, one pedicle cut leaving one long and one short tube graft; *D*, all pedicles cut except at the top and bottom of long "tube graft"; *E*, upper pedicle severed, tube "graft" cut open and sewed in the bed from which the ulcer is removed; *F*, lower pedicle severed, graft cut open and the remainder of the ulcer bed covered.

the same. If it is necessary to expose the tibia, holes about ⅛ inch (3.17 mm.) in diameter should be bored through the bone and into the medullary cavity to allow future granulations to form through these openings. These holes should be about ½ inch (12.70 mm.) apart. It is surprising to see how rapidly the granulation appears through them. Of course, the necessity for boring the holes exists only in rare cases. It is, however, interesting to note that Lanz of Amsterdam (quoted by Matas[10]), in 1906, in trying to obtain "deep lymphatic derivation" in his operation for elephantiasis, trephined holes in the tibia and placed a "number of pediculated strips of the fascia lata" through the opening into the medullary canal. It is well known that holes bored through the outer plate of the cranium,

when the scalp has been removed, will allow granulations to grow through the openings and form the bed for future grafts. The raw area is dressed with perforated rubber, such as is used in protecting skin grafts.

From seven to ten days after the operation, depending on the appearance of the various "tube" grafts, the pedicle of one end of one "tube" graft should be cut about ¼ inch (6.35 mm.)each day until the graft is completely freed except at

Fig. 3.—*A* shows "saddle" ulcer of the leg, the type requiring removal of fascia on both sides of the leg and thigh; *B* shows removal of fat and fascia on the inner side of the thigh and leg, the ulcer being covered with towels; *C*, removal of fat and fascia on the outer side of the thigh and leg, a towel again being used; *D*, step in which the ulcer is exposed and the incision covered, the fat and fascia being removed down to the ulcer; *E*, removal of ulcer with a margin wide enough to find nearly normal tissue; *F*, removal until nearly normal tissue is found, even in some cases through the periosteum of the tibia.

the top near the knee and at the bottom near the ankle. The cut pedicles are rolled and the edges sewed together so as to complete one long tube graft, which should be ample to cover the area from which the ulcer has been removed. It requires experience, as well as common sense, to know when and how rapidly to cut the pedicles; the same is true in releasing the ends of the long tube graft.

From seven to ten days after the operation, depending on the appearance of the various "tube" grafts, the pedicle of one end of one "tube" graft should be cut about ¼ inch (6.35 mm.) each day

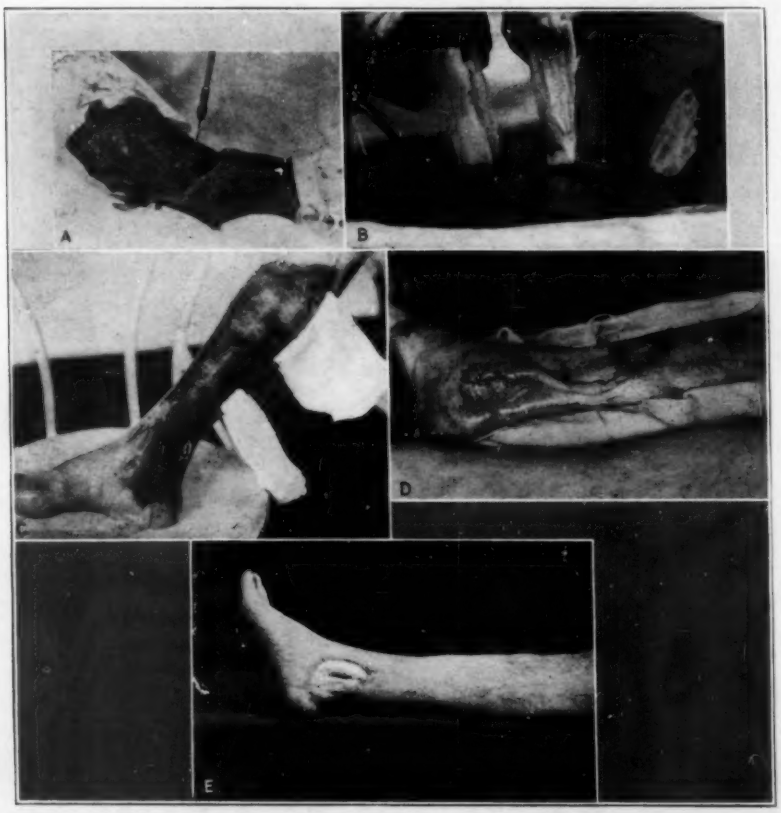

Fig. 4.—Continuation of operative step in removal of "saddle" ulcer: *A*, boring holes in tibia for future granulations; *B*, first step in making a connected series of "tube" grafts, showing three pieces of gauze lifting up three tube grafts, each connected by an intervening pedicle; *C*, one pedicle has been cut leasing one long "tube" graft connected by an intervening pedicle, to lower and shorter "tube" graft; *D*, all pedicles except the lower one have been cut and the upper end of the "tube" graft split and sewed over granulations covering about half of the old ulcer; *E*, the remaining half of the graft is now covered and the site from which the ulcer has been removed completely covered with total thickness skin graft.

until the graft is completely freed except at the top near the knee and at the bottom near the ankle. The cut pedicles are rolled and the edges sewed together so as to complete one long tube graft, which should

be ample to cover the area from which the ulcer has been removed. It requires experience, as well as common sense, to know when and how rapidly to cut the pedicles; the same is true in releasing the ends of the long tube graft.

When ready for the graft, a Kelly clamp is applied to the upper pedicle and left on for ten minutes. The clamp is closed to the first serration of the lock. The next day the same procedure is carried out and the clamp closed to the second serration of the lock. This testing is continued until the surgeon can feel sure that the lower pedicle will take care of the circulation of the entire graft. After the top pedicle is severed, the graft is split for the proper length in its long diameter, turned down and sewed to the sides of the raw surfaces from which the ulcer has been removed. As soon as this is well healed, the lower end of the tube graft is cut and the graft split so as to be flattened out and cover the remainder of the raw surface.

It has been my experience that the total thickness graft is more satisfactory than the "pin," or Davis, graft. However, for various reasons, if one is not able to obtain the total thickness graft, the "pin" graft is easily and successfully applied. It is interesting to note that if there is any "break" or recurrence of the ulcer, it does not occur in the graft, but in the margin where the epithelium comes out from the periphery. In fact, I have used the total thickness graft only in eight cases, the rest has been "pin" and Thiersch grafts. In four cases I have successfully employed large Thiersch grafts at the time of primary operation. It is usually necessary to allow the granulations to come from around the edges and up through the holes in the tibia before the surface is ready to receive the "pin" grafts.

After the grafts have "taken," it is important to see that the patient does not put the leg in a dependent posture until the proper time. It is best to let these patients start by hanging the leg down for about an hour or until a faint cyanosis occurs. This method of "testing" the leg allows the patient slowly to resume his duties. However, I believe it wise in all these cases for the patient to use an elastic bandage or Unna's paste stocking for at least six months after leaving the hospital.

SUMMARY

1. The operation advocated is applicable only to extensive or multiple ulcers, particularly to those of many years' duration and associated with much swelling. (In some of these cases numerous unsuccessful operations on varicose veins have been performed.)

2. The operation advocated is simply the application of the method presented by Kondoleon in his treatment for elephantiasis plus wide excision of the ulcer and the employment of total thickness skin grafts when possible. Many of these cases are both clinically and histologically somewhat similar to elephantiasis.

3. The clinical results reported indicate that there is either a regeneration of the lymph channels or a rapid establishment of a collateral lymphatic circulation. The experimental work of others confirms both views.

4. In addition to the operation advocated, it is necessary to be certain that proper attention has been given the venous system,

especially the ligation of the "perforating" veins. The three tests for determining the condition of the veins are all useful and should be employed when possible.

5. In two cases in which periarterial sympathectomy was tried, the results did not seem to verify the claims of the healing or the sterilization of the ulcer.

6. Injection of alcohol close to the ulcer for relief from pain or the intravenous administration of various solutions for the cure of varicose veins associated with ulcers appears to me surgically unsound.

7. Much interesting and instructive work has been inspired by the late Dr. W. S. Halsted and his co-workers concerning the origin, development, function and regeneration of the lymphatic system. Much of this work was done while trying to ascertain the cause of the swelling of the arm which sometimes follows operations for cancer of the breast.

8. There are only 142 cases of the Kondoleon operation for streptogenic elephantiasis reported in the literature, though there must have been many hundreds of others not reported.

9. The polyvalent vaccine of streptococci has not proved of any benefit in the condition discussed either for cure or for prevention of recurrences. It is possible that the technic of either Burbank or Baer might prove of aid in obtaining an effective autogenous vaccine.

10. The cure of phlegmasia alba dolens ("milk leg"), either with or without ulcers, requires a more extensive removal of fascia.

11. This report is based on twenty-seven cases, in twenty-six of which the ulcer was cured and there was marked relief of pain and edema. One patient died from an epithelioma, forming in the grafted area. This patient refused the employment of radium. All the rest of the patients have returned to their former occupations.

RADIOSENSITIVE INTRA-ORAL TUMORS

A CLINICAL STUDY *

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It is the purpose of this study to call attention to a group of malignant epithelial tumors which may be separated from the general class of epidermoid carcinomas because they present peculiar clinical manifestations, a specific histologic structure and a remarkable susceptibility to radiation. A notable variation in the natural history of certain intra-oral tumors has been previously observed. Thus, Ewing [1] stated that within the group of epidermoid carcinomas, particularly of the tonsil, base of the tongue, nasopharynx and larynx, cases occur which show a high degree of malignancy and run an unusually rapid course. The peculiar histologic structure of these tumors, notably the absence of squamous features and the presence of transitional epithelial characters has also been noted. In 1921, Regaud recognized the peculiar microscopic changes and radiosensitivity of certain tonsillar and nasopharyngeal tumors. He was impressed with a close and constant relation between the epithelial and lymphoid elements and, on account of the resemblance of this structure to normal lympho-epithelial tissue, applied to them the term "Lympho-epitheliome." The case presenting these unusual histologic features was reported by Reverchon and Coutard [2] and concerned a tumor of the hypopharynx which showed a marked response to radiation. At about the same time (1921), Schmincke [3] reported several cases of carcinoma of the tonsil and nasopharynx which displayed an unusual susceptibility to radiation and a structure similar to that described by Regaud; these he also designated as "Lympho-epitheliome."

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* From the Department of Intra-Oral Diseases, Dr. Douglas Quick, Chief Surgeon.

1. Ewing, J.: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1928.

2. Reverchon, L., and Coutard, H.: Lympho-épitheliome de l'hypopharynx traité par la roentgen thérapie, Bull. et mém. Soc. d'oto-rhino-laryngologie, congrès, 9 Mars, 1921.

3. Schmincke, A.: Ueber lympho-epitheliale Geschwülste, Beitr. f. path. Anat. **68**:161, 1921.

In 1923, Mlle. Derigs [4] reported a case of lympho-epithelioma of the pharynx with metastases to the vertebral column and abdominal viscera, in which the structure of the metastatic tumors was described as being composed of undifferentiated cells infiltrated by lymphocytes and resembling the original tumor.

That the peculiar clinical manifestations of these tumors were previously recognized is shown in a publication by New [5] in 1921, in which the syndrome of malignant tumors of the nasopharynx is described. He noted the difficulty of detecting the primary lesion, pointed out the frequency with which the metastases in the cervical nodes were erroneously regarded as the primary tumor and the necessity for a careful search elsewhere for a small and hidden primary focus.

The peculiar clinical manifestations of tumors of the nasopharynx were also described in 1923 by Crowe and Baylor [6] who reported a series of cases and demonstrated by means of excellent illustrations their special histologic structure. These authors pointed out the structural resemblance between these tumors and the sarcomas and emphasized the difficulty in the histologic differentiation of the two processes.

In 1925, Quick and Cutler,[7] studying changes in tissues due to irradiation, reported their observations on a series of metastatic tumors in cervical lymph nodes. It was noted that certain epidermoid carcinomas, especially of the tonsil, base of the tongue and nasopharynx, presented a specific histologic structure, displayed a marked susceptibility to radiation and pursued an unusual clinical course. The term transitional cell epidermoid carcinoma was applied to these tumors. This report was followed by a further clinical and pathologic study of twenty cases observed over a period of three years, with several observations [8] obtained at autopsy.

Jovin,[9] in 1926, reported a series of cases from the Radium Institute of Paris and described the clinical, pathologic and radiotherapeutic features of the disease. This author expressed the belief that these

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4. Derigs, P.: Lymphoepitheliales Carcinoma der Rachens mit Metastasen, Virchows Arch. f. path. Anat. **24**:1, 1923.

5. New, G. B.: Syndrome of Malignant Tumors of the Nasopharynx, J. A. M. A. **79**:10 (July 1) 1922.

6. Crowe, S. J., and Baylor, J. W.: Benign and Malignant Growths of the Nasopharynx and Their Treatment with Radium, Arch. Surg. **6**:429 (March) 1923.

7. Quick, D., and Cutler, M.: Radiation Reaction of Metastatic Squamous Cell Carcinoma in Cervical Lymph Nodes, Am. J. Roentgenol. **14**:529, 1925.

8. Quick, D., and Cutler, M.: Transitional Cell Epidermoid Carcinoma, a Radiosensitive Type of Intraoral Tumor, Surg. Gynec. Obst. **45**:320, 1927.

9. Jovin, J.: Les lympho-epitheliomes du pharynx, Ann. d. mal. de l'oreille, du larynx., 1926, vol. 45.

tumors arise from the lympho-epithelium occurring normally in these locations. The high degree of malignancy, rapid and widespread metastases and marked susceptibility to radiation are emphasized as the essential clinical features of the disease.

HISTOLOGIC STRUCTURE

The microscopic structure of the group of tumors which I have described presents the following two fairly distinct histologic types: (*a*) Lympho-epitheliomas, forming a small proportion of the cases, are recognized by the syncytial masses and rich infiltration with lymphocytes. (*b*) Transitional cell carcinomas, the more common variety, present the features of anaplastic epidermoid carcinoma; in these, the epithelial characters are distinct and lymphocytes are absent.

It remains for further investigation to determine whether any clinical differences can be demonstrated between these two histologic varieties. In a certain small proportion of cases, the histologic structure does not permit a differential diagnosis between lympho-epithelioma, transitional cell carcinoma and lymphosarcoma, since the cells are loose and broken up as in lymphosarcoma. In these cases, the diagnosis may sometimes be reached only after careful consideration of the clinical observations in conjunction with the microscopic picture. It is particularly to be noted that all these types are highly radiosensitive and can readily be distinguished from squamous carcinoma, both histologically and clinically.

Lympho-Epithelioma.—A small proportion of tumors of the tonsil and nasopharynx present a structure which coincides with those tumors described by Regaud and by Schmincke as "lympho-epithelioma." In these cases, the structure shows epithelial cells in wide sheets and cords growing diffusely and infiltrating the surrounding lymphoid tissue. The cells are large, pale and delicate with a thin cell membrane. The protoplasm is ill defined, has a trabeculated arrangement and often forms a true syncytium. The nuclei are large, clear and pale, and show marked variation in size. Nucleoli are prominent and mitoses abundant. In places, the lymphocytic infiltration is so thick that the tumor cells are hardly visible through the lymphoid structure. Occasionally, one sees larger cells in the reticulum, round or polyhedral, with hyperchromatic nucleus and sometimes multiple nuclei.

The structure in general strongly suggests primary endothelioma and is often difficult to distinguish from reticulum cell lymphosarcoma. The intimate association between the clear endothelial-like cells and the lymphoid tissue suggests an origin from lympho-epithelium as described by Jolly and forms the basis for the term lympho-epithelioma. This structure is relatively rare. In a review of 300 tumors of the base of the tongue, tonsil and nasopharynx, only nineteen, or 6.3 per cent, were found to fall into this group (Ewing).

Transitional Cell Carcinoma.—The structure to which this term has been applied shows mainly small round and polyhedral cells with relatively large hyperchromatic nuclei which occupy almost the entire cell. The cells vary markedly in size and staining intensity, and mitoses are abundant. The cells grow diffusely in cords and sheets and infiltrate the surrounding lymphoid tissue. The arrangement is sometimes plexiform. There is little intercellular connective tissue. Polymorphonuclear leukocytes, lymphocytes and plasma cells are numerous. The cells show marked loss of differentiation, and squamous characters are entirely lacking. These tumors sometimes reach a high grade of anaplasia, so that the growth is diffuse and the epithelial characters of the cells almost lost. This structure often approaches the appearance of lymphosarcoma so closely that a differentiation between the two processes may be difficult.

The metastatic tumor in the cervical lymph nodes usually has a structure similar to that of the primary tumor. Rarely, some traces of squamous characters are found, although more often the metastatic process tends to become more undifferentiated. Invasion of lymphatics and blood vessels in the primary tumor by groups of tumor cells is often encountered and accounts for the early involvement of the lymph node in these cases. Tumors presenting this structure are more common than lympho-epitheliomas and occur less frequently than squamous carcinomas. They comprise approximately 10 per cent of epitheliomas occurring in these regions.

The similarity in the histologic structure between these tumors and radiosensitive tumors in other locations is noteworthy. The esophagus is sometimes the seat of anaplastic epidermoid carcinomas presenting the structure, clinical course and radiosensitivity of transitional cell carcinoma. In a study of 200 cases of carcinoma of the cervix, it was found that 20 per cent were highly cellular anaplastic tumors presenting all the histologic features of this group.[10] In the clinical course and sensitivity to radiation, this type of carcinoma also simulates the intraoral group. These observations lend support to the belief that in all these groups one is dealing with radiosensitive anaplastic epidermoid carcinomas which present a uniform and characteristic structure and are accompanied by a definite clinical course.

HISTOGENESIS

Although the exact origin of these tumors is not definitely known, several possible sources suggest themselves. In this discussion, it is important to reemphasize the distinction between true lympho-

10. Healy, W. P., and Cutler, M.: Relation Between Structure and Prognosis in Cervical Carcinoma Under Radiation Treatment, Am. J. Obst. & Gynec. **16**:15, 1928.

epithelioma and transitional cell carcinoma, as there is considerable evidence in favor of the view that each variety may have its own source of origin. The view held by Regaud, Schmincke, Lacassagne and others

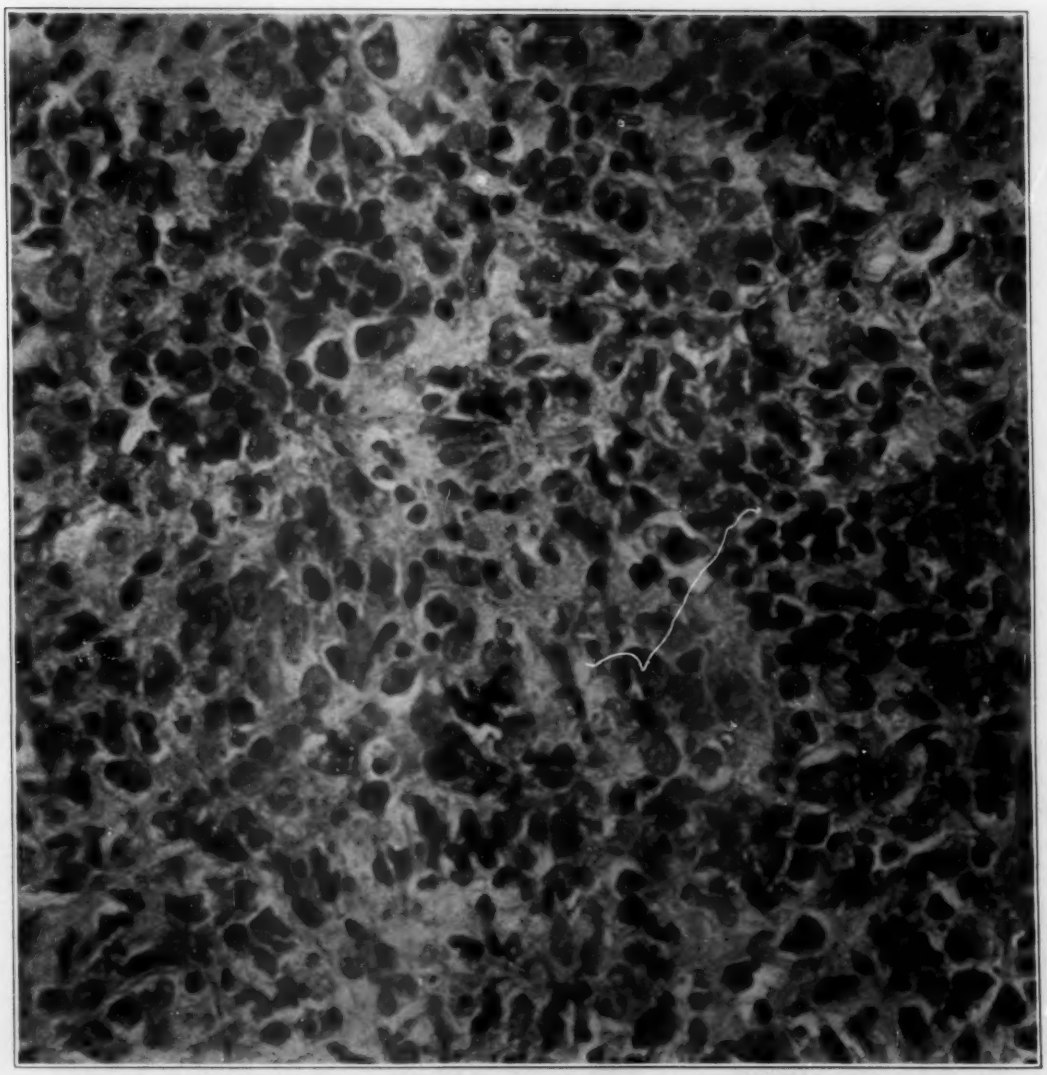

Fig. 1.—Showing the structure of lympho-epithelioma. Note the large, clear endothelial-like cells infiltrated with lymphocytes. Biopsy specimen from ulcerated lesion of tonsil.

is that lympho-epitheliomas arise from squamous epithelial cells which are in close contact with and often infiltrated by lymphoid tissue to which the term "lympho-epithelium" was applied by Jolly. These authors are

of the opinion that the essential feature of the histologic structure of these cells is an intimate association of endodermal epithelium with lymphocytes. Evidence in favor of this view is found in the prevalence of tumors presenting this structure in locations in which lympho-epithelial tissue is described, namely, the tonsil, base of the tongue and

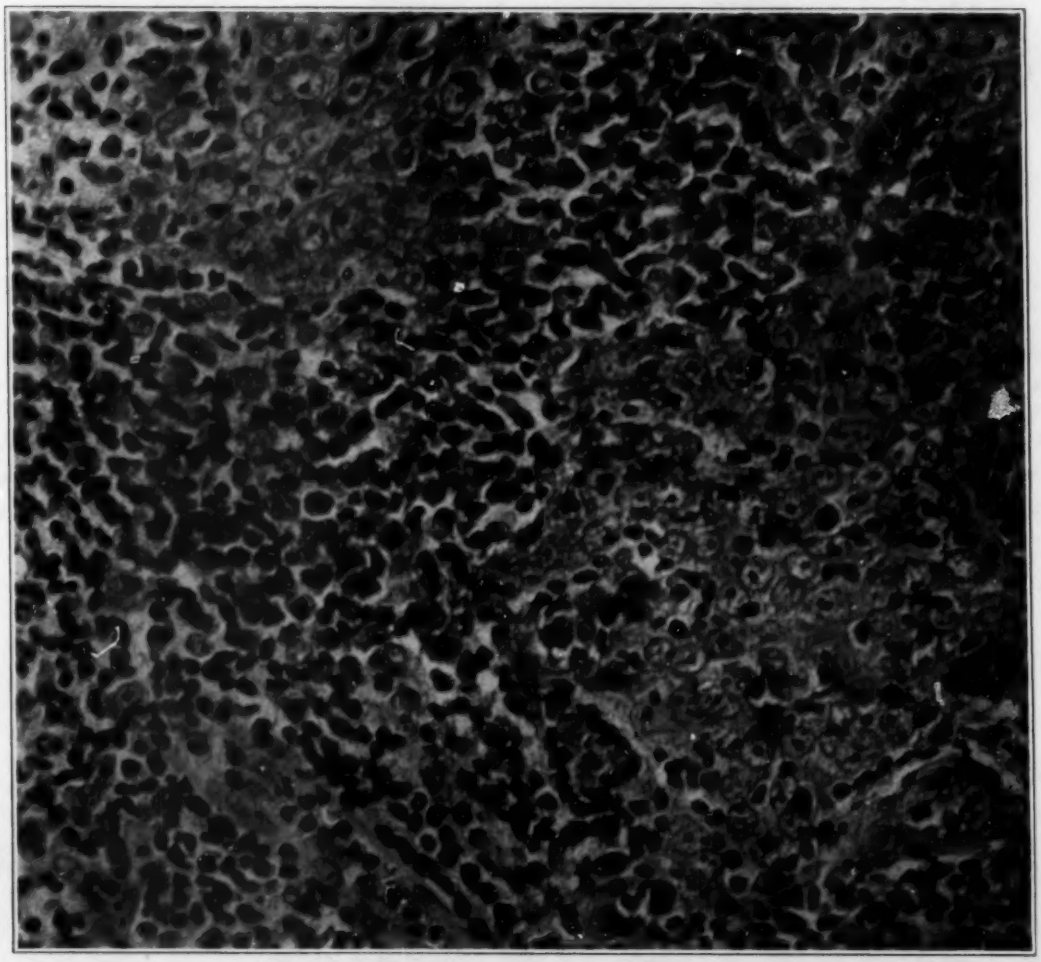

Fig. 2.—Lympho-epithelioma of superior nares showing large, clear, pale nuclei and prominent nucleoli. Note the thick infiltration with lymphocytes.

nasopharynx. On the other hand, it is pointed out by Delbet and others that the exact rôle of the lymphocytes in the histologic structure is not fully known.

Whereas it is possible that lympho-epitheliomas arise from a special tissue, it is altogether probable that anaplasia rather than a special cell

of origin accounts for the peculiar histologic features of transitional cell carcinoma. This view gains support in the fact that a relatively high proportion of tumors of the tonsil, base of the tongue, pharynx and larynx are distinctly squamous in character and also in the occasional

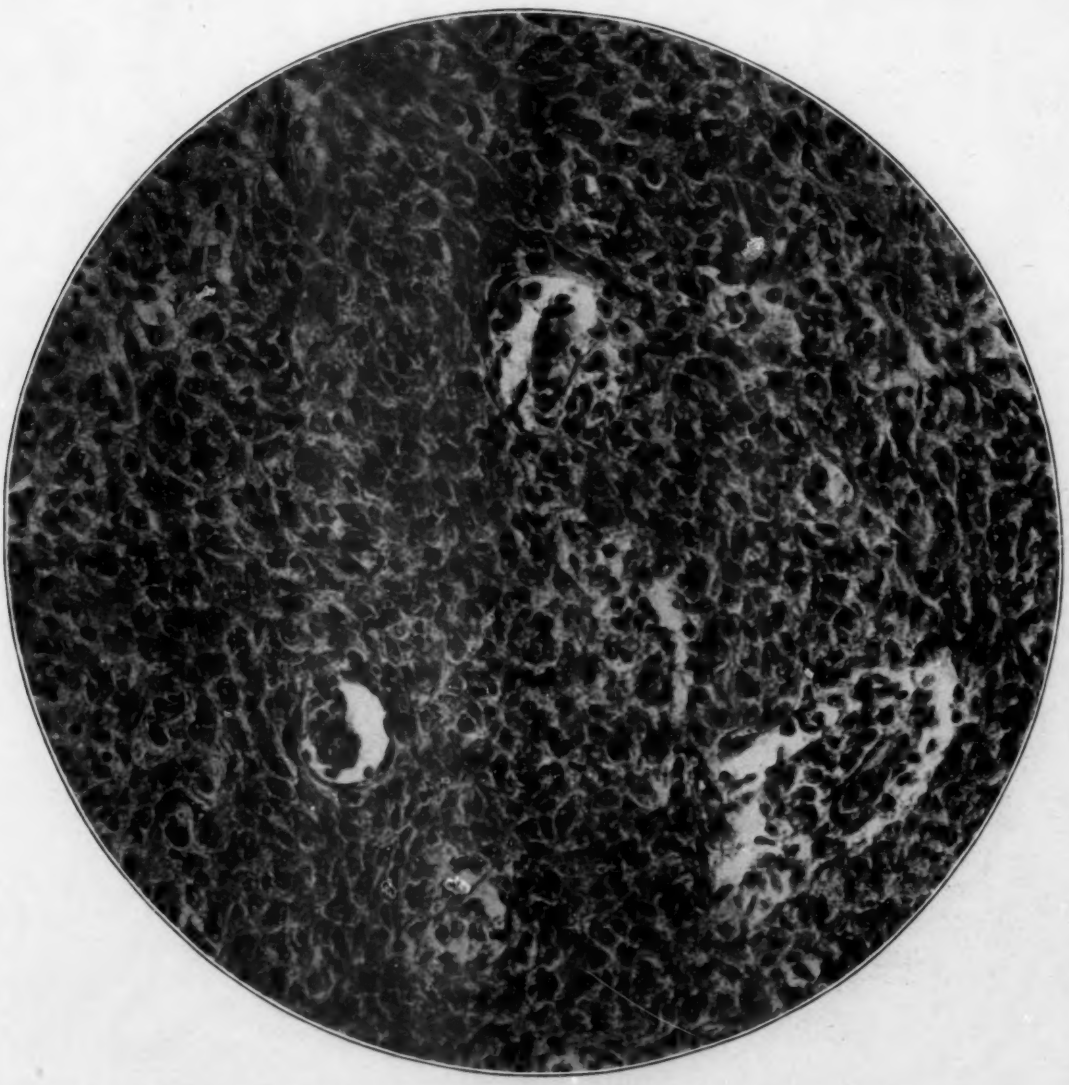

Fig. 3.—Showing the structure of transitional cell carcinoma. The tumor shows small, round and polyhedral cells with hyperchromatic nuclei growing in cords and sheets. Biopsy specimen from lesion of nasopharynx.

presence of highly undifferentiated cells in growths which are essentially squamous.

Since it is the essential purpose of this study to call attention to the clinical features and therapeutic aspects of this disease, it is not within

the scope of this paper to enter further into the details of their histogenesis. The complexity of this phase of the problem calls for special histologic investigations into the exact origin of these tumors, a point which for the present must be regarded as still unsettled.

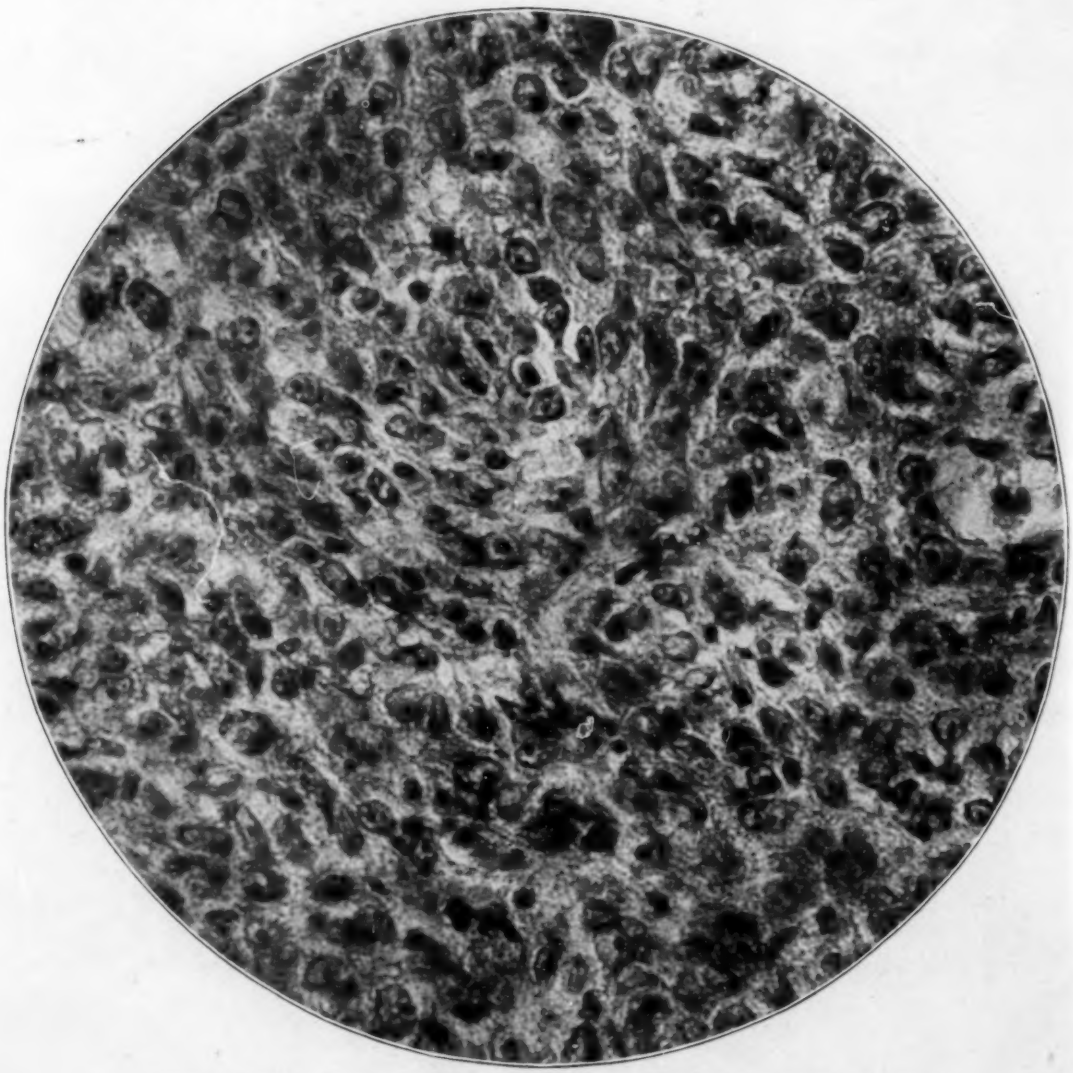

Fig. 4.—High power view of figure 3. There are no definite squamous features. Note also the absence of lymphocytic infiltration.

PRIMARY LESION

The common locations of the primary tumor are the pharyngeal tonsil, lingual tonsil, base of the tongue and nasopharynx. The larynx and esophagus are not infrequently the seat of anaplastic and radiosensi-

tive tumors which may be classed in this group. The primary focus is usually small and frequently insignificant in its proportions. It presents, on inspection, a finely granular surface suggestive of erosion, rather than frank ulceration. In some instances, especially in the early

Fig. 5.—Necrotic tumor tissue in cervical lymph node, the seat of metastatic lympho-epithelioma after moderate external irradiation. Primary lesion in tonsil (fig. 1).

stages of the disease, there have been neither erosion nor ulceration but rather the appearance of fixation of the mucous membrane over a mass beneath it. The lesion is usually flat and gives the impression of having

taken its origin in the deeper structures and then adhered to and eroded the mucous membrane from beneath. Sometimes, the lesion is diffuse, extending around the pharyngeal ring and involving the mucous membrane of the base of the tongue, tonsils and posterior pharynx with superficial ulceration and bilateral cervical adenopathy. In several cases, the primary lesion in the tonsil has consisted of a tumor, as large as a hen's egg, projecting across the midline and causing interference with breathing and swallowing.

CERVICAL ADENOPATHY

Early metastatic involvement of the cervical lymph nodes is one of the most constant and characteristic features of this disease. In only a few early cases has this been absent when the patient first came under observation. The cervical nodes, at first small, grow rapidly and soon form a bulky mass. The location varies somewhat but usually is in the middle and upper cervical regions beneath and in front of the sternomastoid muscle and reaching upward to the lower lobe of the ear. The consistency is perhaps firmer than that of lymphosarcoma but lacks the induration of squamous carcinoma. The tumor process has a greater tendency to remain encapsulated than does squamous carcinoma, remaining more or less freely movable except in the later stages. Perforation of the capsule is sometimes seen, but spontaneous ulceration has not been observed. The usual history accompanying these cases is that for six, eight or ten months a cervical mass has been noted; and in several cases the presence of a mass for as long as from one to three years has been established. An interesting and unusual feature of these tumors is the occasionally long period of quiescence of the cervical adenopathy. The stimulus to further activity usually has been some acute infection in the nose, mouth or throat. At first unilateral, the adenopathy soon extends and involves the opposite side of the neck. A bulky cervical adenopathy, however, may remain unilateral for many months. In the early stage of the disease, pain is nearly always absent; in the more advanced stages, the bulky mass begins to cause pressure symptoms. The pain is sharp, and is often referred to the ear, postauricular and occipitoparietal regions.

VISCERAL METASTASIS

Visceral metastasis is of frequent occurrence in this variety of tumor, in marked contrast to the extreme rarity of distant metastasis from intra-oral squamous carcinoma. The liver and retroperitoneal lymph nodes have been found to be the seat of bulky metastatic tumors from small primary intra-oral lesions. Metastasis to bone is reported by Jovin, who observed patients showing clinical and roentgenologic signs of metastasis to the vertebral column. On account of the absence of definite evidence at autopsy, however, the author leaves this question open to further

study. Through the courtesy of Dr. Scoville, it was my privilege recently to study specimens of a nasopharyngeal tumor showing the typical feature of lympho-epithelioma which produced metastases in the bones of the ankle and the elbow. Tissue taken from the metastatic deposits in the ankle showed the same histologic structure as the primary tumor. This observation is, therefore, in accord with the reports of Jovin and others in regard to this mode of dissemination.

That the disease may progress for long periods without visceral involvement is demonstrated by several cases in which the primary lesion and cervical adenopathy had been present from one to two years without clinical evidence of visceral metastasis. Further evidence of this is shown by the absence of visceral metastases in several autopsies on patients who succumbed to the disease from one to three years after the onset of symptoms. In one patient, acute intestinal obstruction developed as a result of pressure of a large mass of retroperitoneal lymph nodes on the splenic flexure of the colon. The other patient presented large multiple tumors in the liver and retroperitoneal nodes at autopsy.

Whereas the microscopic structure of the cervical node metastases is usually similar to that of the primary tumor, the structure in the visceral deposits often assumes more anaplastic feaures. In one case, the hepatic tumor presented an extremely cellular anaplastic structure strongly resembling lymphosarcoma, whereas the primary lesion showed the typical appearance of lympho-epithelioma. This phenomenon is known to occur in other tumors in which the metastatic process appears to have taken on an added growth potential and displayed a more undifferentiated and anaplastic structure.

CLINICAL COURSE

The clinical course of this group of tumors is as characteristic as the histologic structure and differs from that of other tumors in these locations. In my experience, more patients have sought advice regarding a mass in the neck than for intra-oral symptoms. The appearance of large cervical nodes, while the primary intra-oral tumor remains undetected, is one of the notable peculiarities of this disease. A careful search for the primary lesion may reveal a small hidden tumor in the base of the tongue, tonsil or nasopharynx. On the other hand, thorough search may fail to reveal the primary growth. It would seem that the logical explanation for this course of events is that the lesion being deep-seated and the tumor cells of a type which metastasize early, the cervical metastases appear and grow before the primary tumor reaches the surface and ulcerates. Ulceration, pain and bleeding may not occur until late in the disease. In the meantime, the clinical setting is dominated by the metastatic process, and the cervical adenopathy presents the picture of a primary disease of the lymph nodes. The failure to detect

the primary growth leads to various erroneous diagnoses, including branchiogenetic carcinoma, endothelioma, lymphosarcoma, tuberculous adenitis or simple chronic lymphadenitis. Soon afterward, the mucous membrane becomes ulcerated, and pain and bleeding direct attention to the primary focus.

Analysis of the clinical features of a series of twenty cases showed that thirteen patients had noted enlarged cervical nodes as the first sign of disease before any abnormality referable to the intra-oral region was detected. In five patients, thorough search failed to reveal a primary intra-oral lesion, and the disease progressed under various diagnoses of primary diseases of the lymph nodes.

The peculiar clinical course of this disease has been noted by other investigators. In a clinical study of carcinomas of the nasopharynx, Crowe and Baylor stated that the first sign of carcinoma in this region is often a painless and rapid increase in size of the deep cervical nodes at the angles of the jaw. In seventy-nine cases of carcinoma of the pharynx reported by New, fifty-one of the patients had enlarged cervical nodes. Eighteen of the fifty-one patients in whom the cervical nodes were involved had had operations on the neck without discovery of the primary tumor. A microscopic diagnosis of endothelioma of the lymph nodes had been made in three cases. My former impression that the course of the disease is always rapid and soon leads to fatal termination was based on the fact that most of the patients when first seen had been subjected to one or more incomplete operations. An opportunity to observe several cases in which the disease had been permitted to pursue an undisturbed course has demonstrated that the natural course may sometimes be extremely slow.

DIFFERENTIAL DIAGNOSIS

Lympho-epithelioma and transitional cell carcinoma must be differentiated from squamous carcinoma, lymphosarcoma, branchiogenetic carcinoma and endothelioma. Although typical cases may be recognized clinically, a differential diagnosis may be extremely difficult and possible only with the aid of a biopsy.

In its generalized secondary extensions and wide dissemination, as well as its prompt and rapid response to radiation, this disease simulates lymphosarcoma more nearly than it does the group of epidermoid carcinomas. Lymphosarcoma is more raipd in its course, tends to appear bilaterally in the early stages of the disease and soon produces constitutional symptoms. The response to radiation does not permit differentiation as the two tumor processes are about equally radiosensitive. Lymphosarcoma is often discovered after tonsillectomy.

Although typical lymphosarcoma and transitional cell carcinoma are readily distinguished microscopically, certain borderline structures are

extremely difficult to interpret, and a differential diagnosis based on structure alone may be impossible. In such cases, the clinical observations are of considerable help in the differentiation. Fortunately, an absolute distinction between the two conditions may not be important from a practical standpoint as the treatment is essentially similar in the two diseases.

Branchiogenetic carcinoma is distinguished by its histologic structure. It is nearly always squamous and consequently resistant to radiation. It differs, therefore, in this important respect from the markedly radiosensitive transitional cell carcinoma and lympho-epithelioma. This marked difference in response to radiation may be utilized practically in the differential diagnosis.

Primary endothelioma of lymph nodes may simulate transitional cell carcinoma in which the nodes are enlarged and the primary lesion is undetected. The disease is comparatively rare and commonly arises on the basis of a chronic granulomatous inflammation, especially tuberculosis. It may occur as a systemic involvement of many lymph nodes or as single or multiple tumors of cervical, axillary or other lymphatic chains. The history of an antecedent tuberculous infection, the lack of response to radiation and the persistent failure to find a primary intra-oral lesion are differential points in favor of endothelioma. Ewing stated that a diagnosis of primary endothelioma of the lymph nodes is hazardous and is to be made only by exclusion. Furthermore, it is important to recognize that endothelioma is rare, whereas secondary carcinoma is relatively common.

RESPONSE TO RADIATION-THERAPEUTIC TEST

The marked radiosensitivity of this group of tumors constitutes one of its most characteristic and important properties. It is this feature of the disease that first led to its discovery and recognition as an entity. Rapid regression and disappearance of the primary lesion and cervical adenopathy in response to relatively weak doses of radiation are reported by Regaud, Schmincke, Jovin, Jungling and others.

The mode of regression of this radiosensitive tumor process undoubtedly differs from that of the radioresistant tumors. Destruction of squamous cell carcinoma must occur through an intensive and almost caustic action of interstitial irradiation or by heavy external irradiation, whereas complete primary regression of radiosensitive transitional cell carcinoma or lympho-epithelioma may often be accomplished by means of external irradiation alone. The rapid regression of these tumors is associated with an equal tendency to rapid recurrence if the tumor process is not completely sterilized. The radiosensitivity of these tumors differentiates them sharply from the radioresistant squamous carcinomas and branchiogenetic carcinoma. These differences assume considerable

importance from a diagnostic standpoint, so that external irradiation may serve as a useful means of differentiation in the diagnosis of obscure cervical tumors.

TREATMENT

In a consideration of the method of choice in the treatment for this disease, it is important to emphasize the two properties of these tumors on which the principle of therapy is based: (1) their high degree of malignancy and (2) their marked susceptibility to radiation.

The extremely unfavorable results of surgical intervention in the treatment for highly cellular anaplastic tumors in any location is now becoming universally recognized. The hopeless prognosis of carcinoma of the tonsil under surgical treatment may be attributed largely to the highly malignant nature of the tumor process. The inaccessibility of the primary tumor adds further difficulty to surgical removal. Histologic observations have demonstrated the early tendency of these tumors to invade the lymphatics, a property which accounts for their early and extensive metastasis. Any method of treatment to be successful must be devoid of trauma in order to prevent dissemination of this extremely unstable cellular tumor.

The principles of irradiation in this disease are based on the marked susceptibility of these tumors to this agent. Because of their high degree of malignancy, local recurrence and metastasis invariably follow the primary regression, unless a complete sterilization of tumor cells can be accomplished. This may be affected either by x-rays or radium, or by the two agents combined. If complete sterilization of the tumor process can be accomplished by means of heavy external irradiation alone, this method is to be preferred. In some cases, it has been necessary to add further irradiation by the implantation of gold filtered emanation into the primary lesion. It is believed that the dosage should be the maximum amount of radiation which can be delivered to insure complete destruction of the tumor and still preserve the integrity of the tumor bed.

The ability to care completely for the primary lesion and metastatic cervical nodes by radiation has been demonstrated clinically and microscopically. The danger lies in the early dissemination of the disease to the viscera, so that whereas the primary lesion and cervical metastases have been cared for, the patient returns with bulky visceral metastases. For this there are several possible explanations: (1) failure completely to sterilize the primary lesion or cervical metastases; (2) dissemination of the disease by operative trauma, and (3) the presence of clinically undemonstrable visceral metastases when treatment is instituted. The highly anaplastic nature of the tumor and its high grade of potential malignancy favor the view that when the cervical nodes are

involved minute distant metastases are already present. On the other hand, it would seem that the disease may remain localized in the cervical nodes for some time. This is demonstrated by a number of cases in which a cure has been effected and is supported by evidence obtained at autopsies. Thorough and adequate irradiation in this stage of the disease offers considerable hope of complete sterilization of the tumor and cure of the patient.

TABLE 1.—*Nine Cases of Transitional Cell Carcinoma and Lympho-Epithelioma in which the Patients Have Been Well and Free of Disease More Than Three Years*

No.	Sex	Age	Duration of Condition	Location	Nodes	Biopsy Primary Lesion	Microscopic Examination of Nodes
1	M	53	4 years	Tonsil	+	Transitional cell carcinoma	Invaded
2	F	44	9 months	Tonsil	+	Transitional cell carcinoma	Invaded
3	M	59	10 months	Base of tongue	+	Transitional cell carcinoma	Invaded
4	M	43	6 weeks	Base of tongue	+	Lympho-epithelioma	Invaded
5	M	56	2 years	Tonsil	+	Transitional cell carcinoma	Nodes not removed
6	M	40	2 months	Naso-pharynx	0	Transitional cell carcinoma	No nodes
7	M	44	6 months	Tonsil	+	Transitional cell carcinoma	Invaded
8	M	61	2 months	Larynx	+	Transitional cell carcinoma	Invaded
9	M	59	2 months	Larynx	+	Transitional cell carcinoma	Nodes not removed

	Treatment				
Case	X-Rays	Surface Radium	Bare Tubes	Operation	Result: Free of Disease
1	0	+	+	+	11 years
2	+	0	+	+	9 years
3	+	0	+	+	5 years
4	0	+	+	+	4 years
5	+	+	+	0	4 years
6	+	+	0	0	3 years
7	+	0	0	0	3 years
8	+	+	+	+	4 years
9	+	0	0	0	3 years

RESULTS

It is not possible at this time to give in detail the total number of patients treated. This difficulty is due mainly to the fact that this condition has been recognized as a clinical and pathologic entity only within recent years. It has been possible, however, to select nine patients belonging to this group on whom treatment was begun more than three years ago, who are now well and apparently free from disease. It should be emphasized that this number of patients probably represents but a small percentage of the total number who have been treated. These cases are reported merely to relate the treatment which has been

employed in the patients who have responded well, and to demonstrate that the disease may be controlled by these methods in a small but definite proportion of cases.

Analysis of the important feature in the group of controlled cases shows that four were carcinomas of the tonsil, two of the base of the tongue, two of the larynx and one of the nasopharynx. Six of the patients had involved cervical nodes, confirmed microscopically, and two others had undoubted invasion of the cervical nodes clinically. In only one of the nine cases were the nodes free from disease. Two patients, one with an advanced carcinoma of the larynx and the other with an extensive carcinoma of the tonsil, were free from disease three years after the employment of external irradiation alone. Both had well marked involvement of cervical lymph nodes. One patient with a carcinoma of the nasopharynx without involvement of the nodes was well three years later, after surface irradiation alone. One patient with a carcinoma of the tonsil and extensive involvement of the cervical node was free from disease four years after combined external and interstitial irradiation. The other six patients were treated by combined external and interstitial irradiation and surgical removal of the cervical nodes.

SUMMARY AND CONCLUSIONS

1. Transitional cell carcinomas and lympho-epitheliomas comprise a group of malignant tumors commonly found in the tonsil, the base of the tongue and the nasopharynx and characterized by a peculiar clinical course, specific histologic structure and marked susceptibility to radiation.

2. Although the exact histogenesis of these tumors is not definitely known, it is suggested that each type may have its own source of origin as follows: (*a*) transitional cell carcinoma, from squamous epithelial cells which in their growth have become undifferentiated and assumed anaplastic features; (*b*) lympho-epithelioma, from a special tissue described as lympho-epithelium.

3. The clinical course is characterized by early metastasis to cervical lymph nodes so that the clinical picture is dominated by the metastatic process while the small deep-seated primary lesion remains for a time undetected.

4. The enlargement of the cervical nodes before the primary lesion ulcerates and produces symptoms often leads to erroneous diagnoses of primary disease of the lymph nodes (endothelioma, lymphosarcoma, branchiogenetic carcinoma and tuberculous adentitis). It is important, therefore, thoroughly to exclude a primary deep-seated intra-oral lesion before regarding a cervical tumor as primary in origin.

5. The highly malignant and cellular nature of the tumor process contraindicates surgical intervention alone in the treatment of patients

with this disease. Their marked susceptibility to radiation, on the other hand, renders these tumors especially suitable for radiation therapy.

6. The ability completely to eradicate the disease in the primary lesion and cervical nodes by irradiation alone has been demonstrated. The advisability of surgical removal of the cervical nodes following heavy dosages of radiation is still undecided. Nine cases controlled for over three years by the combined method as well as by irradiation alone are reported.

REPORT OF CASES

CASE 1.—H. B., a man, aged 53, was admitted on April 11, 1917, with the history that about four years before presentation he had noticed an enlarged node on the left side of the neck which had remained quiescent for a long time. About two years before admission, his dentist discovered a mass in the region of the right tonsil which gradually increased in size. Examination showed that the right tonsil was enlarged, nodular and about 3 cm. in diameter. At the angle of the jaw on the right side, there was an enlarged node, 1 cm. in diameter. A specimen taken from the tonsillar lesion was reported on as follows. "Epidermoid carcinoma, papillary and infiltrating, some basal cell features, cells are quite small." Reexamination of this section disclosed the typical histologic features of transitional cell carcinoma. On April 13, radium emanation was applied to the primary lesion as follows: 450 millicuries filtered through 1 mm. of platinum for one and a half hours (total dose, 675 millicurie hours). Three days later, a radium emanation pack was placed over the right side of the neck at a distance of 10 cm., filtered through 2 mm. of lead (1,140 millicuries for ten hours, 11,400 millicurie hours).

On May 8, a dissection of the nodes of the right side of the neck was performed. Microscopic examination showed metastatic transitional cell carcinoma. The largest node was the size of a small hen's egg and was completely replaced by tumor tissue. Sixty millicuries of radium emanation filtered through 1 mm. of platinum was left in the operative wound for four hours (240 millicurie hours). One month later, the tonsillar lesion had completely disappeared, and there was no evidence of cervical adenopathy. There was never any sign of recurrence of the condition in the tonsil or the neck, and the patient became entirely free from disease and in an excellent general condition (eleven years).

CASE 2.—J. R., a woman, aged 44, was admitted on Feb. 4, 1919, with the history that hoarseness and pain on swallowing had developed in 1916. This continued until December, 1918, when a small lump appeared in the left side of the neck, and gradually increased in size. Two years previously, a specimen was taken from the base of the tongue and a diagnosis of sarcoma made. She then received twenty-one roentgen treatments over both sides of the neck. Examination showed the left tonsil to be the seat of a small crater-like ulcer extending onto the tonsillar pillars and the base of the tongue. In the left side of the neck, there was an enlarged node 2.5 cm. in diameter. On Feb. 4, 1919, three glass emanation tubes were inserted into the tonsillar lesion for a total dose of 2,032 millicurie hours, and on April 23, four more emanation tubes were inserted (660 millicurie hours). On Feb. 19, 1919, the enlarged node which was found to be adherent to the jugular vein was removed and the vein resected; 20.2 millicuries in bare tubes were inserted into the tumor bed. Histologic examination showed transitional cell carcinoma in the node. There was no local recurrence after treatment was given, and the patient was free from disease after nine years.

CASE 3.—J. M., a man, aged 59, was admitted on Sept. 8, 1922, with a history of soreness on the left side of the base of the tongue for nine months. Two weeks before admission, a biopsy of the lesion of the tongue showed epidermoid carcinoma. Examination showed considerable redness about the anterior tonsillar pillar on the left side adjacent to the tongue. On palpation, there was a small, irregular, indurated growth involving the left edge of the tongue and extending onto the anterior tonsillar pillar. There was no cervical adenopathy. On September 8, eleven glass emanation tubes were inserted into the primary growth (1,584 millicurie hours). There was prompt regression and disappearance of the primary lesion. On September 8, the patient was given one low voltage roentgen treatment over the right side of the neck, and on September 14, a similar exposure over the left side. On November 1, a node appeared on the left side of the neck; ten days later it was removed, and five glass emanation tubes were buried in the tumor bed. Ten months later, a recurrence was noted in the left side of the neck. The mass was exposed, and twenty glass emanation seeds were distributed throughout (2,439 millicurie hours). Microscopic examination of the cervical node showed metastatic transitional cell carcinoma. The cervical mass responded promptly and disappeared. There was no evidence of disease four and a half years afterward.

CASE 4.—F. N., a man, aged 43, was admitted on Jan. 29, 1924, with a history of dysphagia for ten months. One month before admission, a node was removed from the left side of the neck which on section proved to be carcinoma. Examination showed a bulky growth involving the entire epiglottis and adjacent portion of the tongue. There was a healed scar over the left side of the neck and a diffuse swelling of the soft parts, but no distinctly palpable nodes.

On January 31, nine emanation tubes were inserted into the primary growth for a total dose of 530 millicurie hours. On the two successive days 10,000 millicurie hours of emanation was given over each side of the neck with the radium pack, and one day later a dissection of the left cervical node was performed. Ten emanation tubes were distributed throughout the tumor bed after the complete block dissection (total dose, 1,605 millicurie hours).

Examination of the specimen from the left side of the neck showed muscle, jugular vein and several lymph nodes. One node, 2 cm. in diameter, was found to be replaced by opaque tumor tissue. The other nodes were free. Microscopic examination showed lympho-epithelioma. The primary lesion promptly disappeared, and there was no evidence of disease four years afterward.

CASE 5.—W. B., aged 56, admitted on Sept. 6, 1924, complained of pain on swallowing and of an enlarged node on the left side of the neck, both of six weeks' duration. On examination the left tonsil was found to be enlarged and markedly inflamed with purulent material exuding from the crypts. It was firm and indurated. In the left side of the neck below the angle of the jaw, there was a hard movable node 2 by 2 cm. and a smaller node of the same character. A biopsy specimen from the tonsil showed transitional cell epidermoid carcinoma. The primary lesion was treated with ten glass emanation tubes (1,108 millicurie hours). On September 17, one week later, the patient received one high voltage roentgen treatment over the left side of the neck and the following week a similar dose over the right side of the neck. There was prompt and rapid regression of the primary lesion and metastatic nodes, so that three weeks later there was no evidence of disease in the left tonsil, and the cervical mass was distinctly smaller. On October 3, an incision was made over the left sternomastoid muscle exposing an adherent mass of nodes in the upper deep cervical chain. The internal jugular vein was clamped and divided both below and above the nodes. It was then found

that the mass was so adherent to the deeper structures, especially the carotid artery, that it was considered inoperable. Twelve millicuries of emanation tubes were distributed throughout the mass. One accessible node was removed for microscopic study and showed transitional cell carcinoma. The wound was closed. The following postoperative irradiation was given during various periods when there seemed to be a slight increase in fulness over the operative field. Treatment was followed by prompt regression in each instance. The tonsillar lesion was completely healed, and there was no evidence of disease in the neck four years after operation.

CASE 6.—N. S., a man, aged 40, was admitted on May 20, 1925, with the history of severe headaches, nasal discharge and nasal obstruction developing in January, 1923. In June, 1923, a nasal operation was performed which resulted in temporary relief of the nasal obstruction. One radium treatment in the nasal passages resulted in partial relief of symptoms, but the nasal discharge and

TABLE 2.—*Postoperative Irradiation*

	Radium							
Date	Number of Millicuries	Time of Application	Millicurie-Hours	Area, Sq. Cm.	Filter, Mm. of Silver	Target Skin Distance, Cm.	Location	Application Method
3/11/25	1,559	1 hr. 35 min.	2,500	20	0.5	3	Upper part of neck	Tray
3/18/25	1,980	1 hr. 18 min.	2,500	20	0.5	3	Middle part of neck	Tray
7/ 8/25	1,492	1 hr. 42 min.	2,500	20	0.5	3	Lower part of neck	Tray

	X-Rays					
Date	Time, Minutes	Milli-amperes	Filter	Kil-volts	Target Skin Distance, Cm.	Region Treated
9/29/25	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Left side of neck
10/ 5/25	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Right side of neck
2/10/26	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Right side of neck
2/15/26	80	4	0.5 mm. copper 1.0 mm. aluminum	200	50	Left side of neck

obstruction soon recurred. Several months before admission, a second nasal operation was performed, and observations at biopsy were reported as carcinoma. On examination, the patient presented a bulky tumor filling the nasal passages, more marked on the left side. There was no definite cervical adenopathy. Examination of the tissue removed from the tumor before admission showed transitional cell epidermoid carcinoma. Radiation was administered as shown in table 3.

CASE 7.—L. R., a man, aged 44, admitted on May 18, 1925, had for two months noted soreness and slight bleeding in the left tonsil. Examination showed a large soft swelling of the left tonsil about 2 by 2.5 by 4 cm. The upper half was ulcerated and covered with a grayish slough. In the left upper cervical region, there was a large firm node about 2.5 cm. in diameter. A specimen for biopsy taken from the ulcerated edge of the tonsillar lesion showed transitional cell epidermoid carcinoma. Radiation was administered as recorded in table 4. There was prompt and rapid regression of the primary tumor and cervical node, and the patient remained free from disease until one year later (April 15, 1926) when an enlarged firm node appeared in the right upper cervical region. Radiation was employed as shown in table 5. The node promptly disappeared, and there was no evidence of disease afterward.

Case 8.—W. J. B., a man, aged 61, was admitted in December, 1924, with the history that six months before presentation he noticed a swelling in the right side of the neck. Four weeks before admission, he began to notice difficulty in swallowing. His general health was excellent. Examination showed two enlarged firm nodes in the right side of the neck. Direct examination of the larynx showed a tumor, about 3 cm. in diameter, lying on the pyriform sinus. Five bare tubes totalling 5.1 millicuries were implanted in the primary growth (total, 673 millicurie hours). Following heavy external irradiation with high voltage x-rays

Table 3.—*Irradiation in Case 6*

	Radium						
Date	Number of Millicuries	Time of Application, Hours	Millicurie Hours	Filter, Platinum, Mm.	Distribution, Mm.	Location	Method of Application
5/20/25	41	6	246	0.5	3	Nasopharynx	Platinum bulb
5/22/25	35	6	210	0.5	3	Nasopharynx	Platinum bulb
6/ 4/25	149	6	894	0.5	3	Nasopharynx	Platinum bulb
6/ 5/25	129	3	387	0.5	3	Nasopharynx	Platinum bulb

	X-Rays					
Date	Time, Minutes	Milliamperes	Filter	Kilovolts	Target Skin Distance, Inches	Region Treated
9/14/25	12	4	5 mm. aluminum	125	15	Right side of neck
9/17/25	12	4	5 mm. aluminum	125	15	Left side of neck

Table 4.—*First Course of X-Rays Applied to the Patient in Case 7*

Date	Time, Minutes	Milliamperes	Filter	Kilovolts	Target Skin Distance, Cm.	Region Treated
5/28/25	60	4	0.5 mm. aluminum	200	50	Left side of neck
6/ 4/25	60	4	0.5 mm. aluminum	200	50	Right side of neck

Table 5.—*Second Course of X-Rays Given to the Patient in Case 7*

Date	Time, Minutes	Milliamperes	Filter	Kilovolts	Target Skin Distance, Cm.	Region Treated
4/20/26	12	30	0.5 mm. copper 1.0 mm. aluminum	200	50	Right side of neck
4/23/26	12	30	0.5 mm. copper 1.0 mm. aluminum	200	50	Left side of neck

and the radium pack, a dissection was performed on the right side of the neck. Microscopic examination showed transitional cell epidermoid carcinoma with marked changes due to radiation. The patient's general condition was excellent, and there was evidence of disease after three and one-half years.

Case 9.—F. C., a man, aged 59, in April, 1925, first noticed slight hoarseness associated with some soreness of the throat and a slight cough. On several occasions, he coughed up bloody sputum. His general health remained good, and there was no loss of weight. Examination revealed a granular ulcerated lesion on the right side of the anterior surface of the epiglottis, near the base, extending onto the right vocal cord. In the right side of the neck, underlying the sterno-

mastoid, was a firm movable node, 2.5 cm. in diameter. Examination of a biopsy specimen from the primary lesion revealed a transitional cell epidermoid carcinoma. The case was considered too far advanced for an attempted curative treatment; consequently, it was decided to perform a tracheotomy and resort to surface irradiation as a palliative measure. Radiation was applied as shown in table 6.

TABLE 6.—*Irradiation in Case 9*

	Radium					
Date	Millicurie Hours	Area, Cm.	Filter	Applicator*	Distance, Cm.	Location
1/21/26	2,500	4 by 5	2 mm. brass	"Tray"	3	Right side of larynx
1/27/26	2,500	4 by 5	2 mm. brass	"Tray"	3	Left side of larynx
2/ 8/26	10,000	8 by 12	2 mm. brass	"Pack"	6	Right side of neck
2/ 9/26	10,000	8 by 12	2 mm. brass	"Pack"	6	Left side of neck

	X-Rays †				
Date	Time, Minutes	Kilivolts	Filter	Target Skin Distance, Cm.	Milliamperes
1/25/26	60	200	0.5 mm. copper 1.0 mm. aluminum	50	4
1/27/26	60	200	0.5 mm. copper 1.0 mm. aluminum	50	4

* For the radium "pack," 10,000 millicurie hours at 6 cm. distance is approximately 90 per cent of an erythema dose. For the radium "tray," at 3 cm. distance, 2,500 millicurie hours is approximately 90 per cent of an erythema dose.

† Sixty minutes of "high voltage" x-rays at 4 milliamperes and 50 cm. target skin distance, with the filter as stated before, is approximately 85 per cent of an erythema dose.

Following irradiation, there was marked regression of the primary lesion and the cervical node. Laryngoscopic examination showed marked radium effect and no evidence of disease, the primary lesion having entirely disappeared. The last examination made on July 20, 1927, revealed no evidence of disease in the larynx and complete regression of the cervical node. This is a remarkable case in that the primary lesion apparently disappeared completely under treatment by external irradiation alone. Three years and three months after the beginning of symptoms, there was no evidence of disease locally or generally, and the general condition of the patient was excellent.

EXPERIMENTAL SURGERY OF THE ESOPHAGUS*

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Surgery of the esophagus is of interest if for no other reason than that in spite of the time, energy and ingenuity expended on perfection of the technic it still remains largely an unconquered field. This is evidenced by the appalling mortality attending the more radical operations on this structure. As the literature on the development of esophageal surgery has been reviewed elsewhere,[1] little will be said concerning it here, only the experimental problems pertinent to the subject being discussed.

A combination of several circumstances adds to the difficulties of operation on the esophagus, and often it is accompanied by grave risk. The most significant of the factors which make the problems in operations on the esophagus somewhat different from those in surgical procedures on other parts of the gastro-intestinal tract are: (1) anatomic situation; (2) lack of a true serosa; (3) poor blood supply; (4) physical environment, with particular reference to the movement of respiration; (5) strength and character of the propulsion of food material through it, and (6) lack of an omentum to protect and favor healing of the suture lines.

The esophagus is deeply seated throughout its entire course, so that the problem of exposure was the first to occupy the attention of the surgeon. The exposure of the cervical portion was not so difficult and could be accomplished by deep dissection between the carotid sheath laterally, and the trachea and thyroid gland medially. The exposure of the thoracic portion was much more difficult, as the same difficulties that are found in any intrathoracic procedure were encountered. This portion was first exposed by posterior mediastinotomy in an endeavor to avoid opening the pleural cavity, as the latter procedure was known to be fraught with danger of collapse of the lung and pneumothorax. The exposure of the esophagus through the transthoracic route was attempted, but this method of approach was not put on a safe

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1. Saint, J. H.: Surgery of the Esophagus, Arch. Surg.

basis until the invention of the differential-pressure chamber, and later, and more important, the simple method of intratracheal insufflation. It is thus apparent that surgery of the thoracic portion of the esophagus had been dependent on the development of thoracic surgery. Once the problem of exposure was solved sufficiently well, the other causes militating against successful operation soon attracted the attention of the surgeon.

The esophagus does not possess a serous covering. The significance of this is at once apparent. When the bowel is sutured, the peritoneum, in response to the traumatic irritation imposed on it, throws out lymph which coagulates, thereby sealing the line of suture. This mechanism is lacking in the esophagus and, consequently, the safety of the suture of this viscus is greatly impaired. The outer coat of the esophagus consists of connective tissue continuous with that of the structures surrounding it. When the organ is loosened in its bed, the cellular planes of the neck or the connective tissues of the mediastinum are opened, and a risk is incurred because of the danger of ensuing cellulitis or mediastinitis which may take place in spite of the most careful aseptic precautions. This risk is considerably increased if the lumen of the esophagus is opened, because of the infective nature of the esophageal secretion. Coincident with the danger of mediastinitis is that of infection of the pleura, often leading to virulent empyema.

It is the general opinion that apart from the absence of a serosa, the wall of the esophagus forms poor material for suture, both submucous and muscular coats being cut through easily. In this connection it has been found that if the lower third of an esophagus, recently removed from a patient, is divided and then joined by two layers of fine silk sutures, the artificial juncture withstands the pressure of a column of water 6 feet (182.9 cm.) high without the escape of gas or fluid. From this investigation it is clear that the removed esophageal wall has the required strength; the important point which must be borne in mind, however, is that in the living body the strength of any such line of suture depends entirely on a sufficient blood supply.

Unfortunately, the esophagus is poorly supplied with blood, although it is derived from several arteries, namely, the aorta, the inferior thyroids, the subclavians, the left inferior phrenic and the left gastric. The great danger in end-to-end anastomosis of the esophagus is the constriction of the blood vessels by the sutures, which may result in necrosis with perforation of the wall and leakage of the contents. In some cases, antethoracic subcutaneous transposition of the oral end of the esophagus after resection has interfered sufficiently with the blood supply to cause necrosis.

The movements of respiration are also a complicating factor in surgery of the esophagus. Not only do the respiratory movements make

suture difficult at the time of operation, but they also have a tendency to disturb the site of operation and thus the walling off and healing processes during convalescence. The pull of the diaphragm also places the line of suture on tension, particularly if a considerable length of esophagus has been resected. This complicating factor can be avoided by section of the left phrenic nerve before the esophagus is sectioned.

The passage of food through the esophagus is also slightly different from its passage through the remaining portion of the gastro-intestinal tract from both the physiologic and the surgical standpoints. An inhibitory mechanism often places the intestine at rest after it has been operated on. Apparently, the esophagus is not protected in this manner. The food is propelled into it with great force from the oral cavity; peristaltic waves, controlled by an extrinsic mechanism, then sweep the food toward the cardia. It is thus evident that the ingestion of food and water would place a suture line in the esophagus on considerable tension. The line of suture can be protected from injury by the passage of material within it only by the rigid exclusion by mouth not only of food and water, but of all extraneous material, such as bedding and hair. It should also be recalled that the action of the omentum in protecting the lines of suture in gastro-intestinal operations is an important factor in making operation on this structure possible. Such protection is not afforded a suture line of the esophagus.

The object of the experimental work undertaken was to obtain, if possible, a successful method of suture for the end-to-end anastomosis of the esophagus after simple division, and if this was satisfactory, after resection.

The poor nature of the blood supply in particular was forcibly impressed on us in the earliest experiments on the anastomosis of the divided organ. Fatal cellulitis and mediastinitis were the outcome, and necropsy showed not only sloughing of the cut ends of the esophagus constricted by the sutures, but also discoloration of the mucous membrane for several centimeters above and below the level of division corresponding to the length of the esophagus necessarily isolated for the performance of the operation. As these experimental surgical procedures were carried out with the usual aseptic precautions, it was felt that the primary factor causing the fatal infections was not the contamination of the surrounding tissues with esophageal secretion at the time of operation but the sloughing of the line of anastomosis due to constriction of its blood supply by the sutures with resultant leakage of esophageal secretion.

This led one of us (Saint) to investigate the blood supply to the esophagus in the dog. The most satisfactory method was found to be the injection of a medium opaque to roentgen rays with subsequent

roentgenograms. The specimens to be injected were obtained in a manner similar to that used by Demel [2] in his work on the blood supply to the esophagus of human beings. The method of preparation of the specimens, the technic employed for injection and the results obtained, have been described in detail elsewhere.[1] Briefly, the results obtained were as follows:

1. The roentgenograms showed clearly the scantiness of the blood supply to the esophagus. This was strikingly apparent when the small amount of injection medium capable of filling the arteries of the esophagus was contrasted with the large quantity necessary to fill those of the stomach.

2. The blood supply is segmental in type. Most of the arteries divide into ascending and descending branches, and those of one particular segment anastomose with the arteries supplying the segments above and below.

3. The anastomotic network between the arteries of adjacent segments is scanty.

4. The arteries on reaching the wall of the esophagus pass quickly into its submucous layer and there ramify. Microscopic sections of an esophagus, the arteries of which have been injected, show this layer to be by far the most vascular.

5. According to the distribution of its blood supply, the esophagus may be divided into the following segments: cervical, upper thoracic, middle thoracic, lower thoracic and abdominal.

We shall not discuss in detail the arterial supply to each of these segments. We wish, however, to mention that the parts of the esophagus with the poorest blood supply are the middle and upper parts of the cervical segment and the lowest part of the lower thoracic segment. On the other hand, the middle thoracic segment (at the level of the bifurcation of the trachea) is the most vascular part of the canine esophagus.

As we have mentioned, the ability of a line of suture to hold the two cut ends of any viscus together depends primarily on the conservation of sufficient blood to the line of anastomosis. The studies carried out on the blood supply to the esophagus so clearly demonstrated its poverty as to lead to the conclusion that unless special care was exercised it would be an easy matter to produce enough constriction of the blood vessels by the sutures to cause sloughing of the two cut ends, resulting in extravasation of esophageal secretion with fatal infection.

The structure of the esophageal wall must be taken into consideration also. The muscular coat is not suitable for suture as it will easily tear.

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2. Demel, Rudolf: Die Gefässversorgung der Speiseröhre: Ein Beitrag zur Oesophaguschirurgie, Arch. f. klin. Chir. **128**:453, 1924.

The submucous layer, on the other hand, is strong and its inclusion in the sutures is essential if the two cut ends are to remain in apposition. Aseptic technic and careful packing off of the divided esophagus from the surrounding tissues are a sine qua non.

METHOD OF OPERATION

With the foregoing in mind, a technic was devised for the end-to-end anastomosis of a divided esophagus. A brief outline of this technic has been given elsewhere in a report of the results obtained in a series of simple divisions and anastomoses in dogs. The purpose here is to report a series of operations not only on the divided esophagus but on the organ after resection. The essential special steps in the technic are: (1) the employment of a suture material and a method of suture which would conserve the greatest amount of blood supply to the line of anastomosis; (2) placing the esophagus at rest postoperatively by the prevention of the ingestion of anything for several days while the fluid and food are administered intravenously, and (3) partial elimination of the effect of respiratory movement by section of the left phrenic nerve.

Japanese silk number 1 (which is finer and stronger than the thinnest catgut) was used for the suture on a fine, straight needle, number 12, cut down to about half its original length.

The anastomosis was made by two rows of sutures. In most of the operations the inner row consisted of eight or nine interrupted inverting mattress sutures, spaced evenly around the circumference and passing through the whole thickness of the esophageal wall, thus including the strong submucous layer in their grasp. The needle pierced the wall about 2 mm. from the cut edge, and each suture included in its grasp about 2 mm. of the circumference. Thus, while the blood supply to those parts of the esophageal wall caught in the sutures was constricted when they were tied, that of the remaining greater part of the circumference was unharmed. In some of our later operations interrupted single sutures were used. These are easier to insert, they shorten the time of operation and appear to act as stay sutures as successfully as those of the mattress type. They have the additional advantage of improving the conservation of the blood supply to the line of anastomosis.

The outer row of sutures was continuous, passing through only the muscular coat and avoiding the submucosa where the vessels ramify. This outer row inverted the inner and made the anastomosis water-tight.

The operations of simple division or resection with end-to-end anastomosis were carried out in both the cervical and the thoracic parts of the esophagus. Intratracheal anesthesia was used in all cases.

In the neck a median-line incision was made which extended from the cricord cartilage to the jugular notch, and continued down to the

trachea between the hyoid depressor muscles. It might be mentioned here that this method of approach to the esophagus is much easier than that between the sternomastoid muscle laterally and the hyoid depressor muscles medially. After the pretracheal fascia had been cut through, a finger was inserted backward along the left side of the trachea and hooked around the esophagus which was then brought up into the wound. The recurrent laryngeal nerves, which are adherent to the esophagus, were stripped from it and the viscus isolated by blunt dissection.

The thoracic part of the esophagus was approached by the transthoracic route. The incision was made in the seventh left intercostal space, extending almost from the vertebrae to the sternum, and the rib spreader was inserted. Excellent exposure of the esophagus from the arch of the aorta to the diaphragm was thus obtained. The left half of the diaphragm was paralyzed by the removal of about 1 cm. of the corresponding phrenic nerve, and in this way the postoperative tension on the line of anastomosis due to the movements of the muscle was avoided. Both vagi were dissected free from the esophagus for several centimeters. The isolation of the esophagus was not difficult but could never be accomplished without a hole being torn in the right pleural cavity, because the mediastinum below the hilum of the lung is exceedingly thin in the dog, and the parietal pleurae are so closely adherent to the esophagus that attempts to separate it from them always resulted in their being torn. As soon as the esophagus was isolated for several centimeters in either the cervical or the thoracic region, the operation was continued as follows.

Rubber-covered intestinal clamps were applied to the esophagus above and below the part of its wall to be divided or resected (fig. 1, *a*). These clamps were used only to occlude the lumen of the esophagus and so prevent the escape of secretion into the field of operation from either above or below. The pressure exerted by them was not sufficient to injure the blood supply. After the clamps were applied, the esophagus was thoroughly packed off in a manner similar to that used when gastroenterostomy is to be performed. That part of the viscus between the clamps was then cut through by a scalpel or straight scissors, and the ends turned upward and thoroughly wiped. Then began the application of the technic described for the end-to-end anastomosis of the cut ends of the esophagus. Four or five interrupted inverting mattress sutures were inserted through the posterior half of the circumferences of the cut ends (fig. 1, *b*) ; the clamps were held close together in order to take the tension off the sutures which were then tied (fig. 1, *c*). The anterior halves of the circumferences were then drawn together by four or five similar sutures, each of these being tied before the next was inserted (fig. 2, *a* and *b*). The clamps were taken off at this stage. The second

row, a continuous suture inverting the first, was begun at the center of the anterior part of the line of anastomosis (fig. 2, *c*). Traction toward the left was put on the short end while the suture was continued to the right (fig. 2, *d*). Each bite of the needle included just so much of the esophageal muscular coat as seemed necessary to prevent the cutting

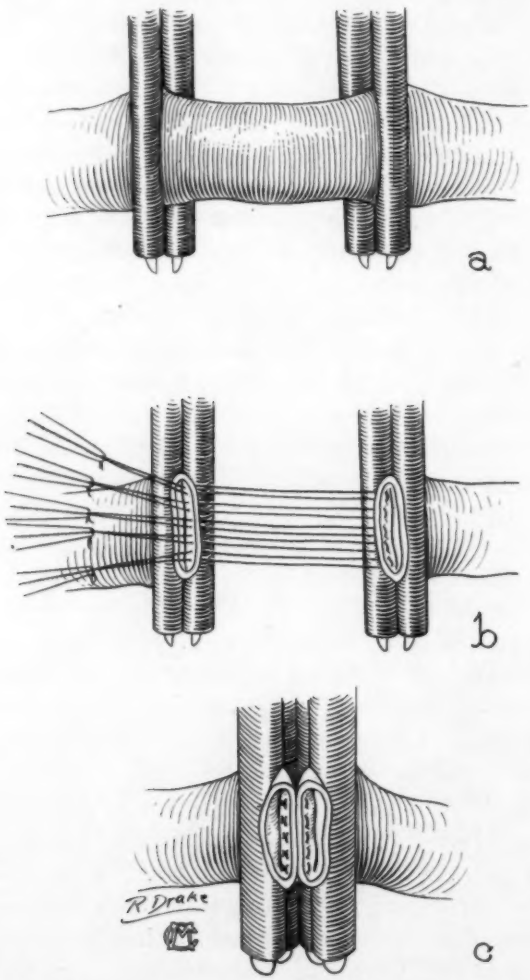

Fig. 1.—*a*, clamps in position; *b*, esophagus resected, mattress sutures inserted in posterior walls of cut ends and ready for tying; *c*, sutures tied, bringing together and inverting the posterior walls of the cut ends.

through of the silk. When a point about half way around the circumference was reached the needle was passed under the esophagus to the left side (fig. 3, *a*). Traction was then exerted on the short end toward the right, and the suture continued from left to right until the starting

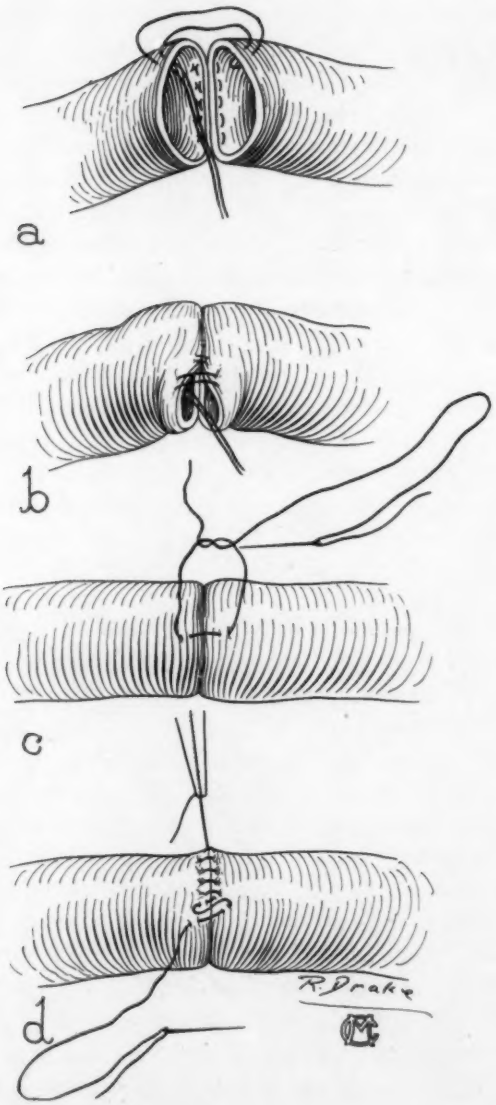

Fig. 2.—*a*, continuation of inverting mattress sutures onto the anterior walls of the cut ends; *b*, completion of inner layer of mattress sutures; *c*, beginning of outer continuous suture in the center of the anterior wall of the esophagus; *d*, suture continued to the right while traction is made on the short end toward the left.

point was again reached (fig. 3, *b*). In this way the entire circumference of the esophagus was sutured with ease. This method of performing the outer continuous suture is technically easier than putting in its posterior half before the introduction of the mattress sutures, as in gastro-enterostomy.

In a few instances the end-to-end anastomosis was performed without clamps. When these were omitted the two cut ends were held in apposition until the inner row of interrupted mattress or single sutures had been inserted by two stay sutures which passed through the entire thickness of the esophageal wall. This procedure did not give better results, and it was technically much easier to work with clamps.

The postoperative treatment is of great importance in the success of the operation. In our experiments it consisted in placing the esophagus at rest for seven days by not giving any food or water by mouth during this period. Water balance and nutrition were maintained by 10 per cent dextrose solution in a physiologic solution of sodium chloride administered intravenously in quantities varying from 200 to 350 cc. a day, according to the weight of the dog. At the end of a week the animal was allowed a mixture of milk and syrup for seven days, after which an ordinary diet was given.

RESULTS

The first six operations in which this technic was used were simple divisions of the esophagus and were carried out on the cervical part at different levels. The following is a summary of the results obtained.

In only one animal did the line of suture slough with an ensuing infection. In the remaining animals the blood supply to the line of anastomosis was conserved sufficiently to prevent sloughing. In the animal in which sloughing of part of the line of anastomosis occurred the operation was performed on the most vascular (lower) region of the cervical part of the esophagus, and as a successful operation was performed later in the same region, the failure can be attributed only to faulty technic. Four of the operations in which the line of anastomosis held successfully were performed on the least vascular (upper and middle) regions of the cervical part of the esophagus.

A small degree of stricture occurred in two animals, probably the result of grasping too much of the circumference of the wall of the esophagus by some or all of the mattress sutures, an imperfection in technic which was remedied later. Two of these animals are under observation and in good condition 376 days after operation (Jan. 1, 1929).

The results of these operations showed that this method of suture permits a supply of blood to the line of anastomosis sufficient to prevent

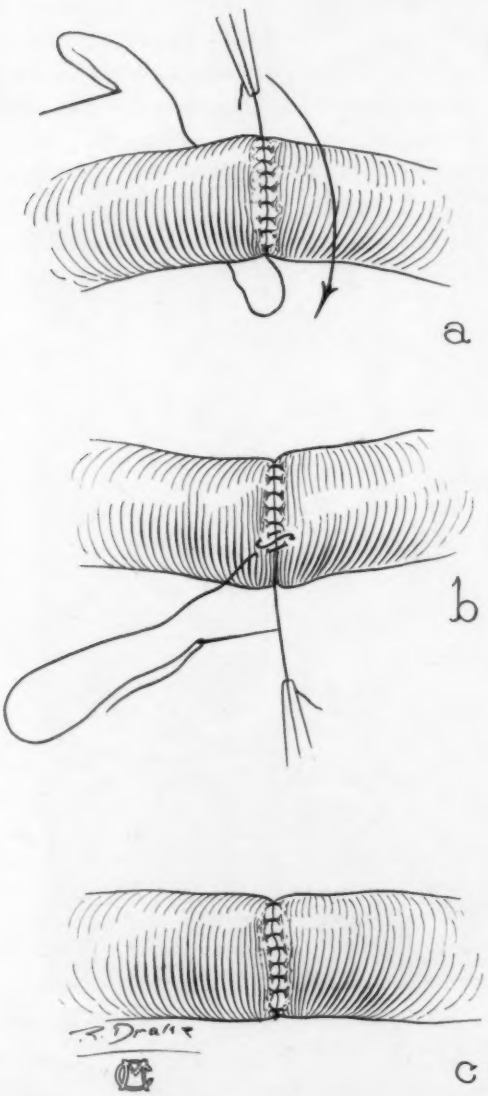

Fig. 3.—*a*, half the circumference has been sutured; the needle is now passed behind the esophagus to the left side and the short end of the suture is drawn over to the right; *b*, traction of the short end toward the right and continuation of the suture from left to right; *c*, anastomosis complete.

sloughing and ensure union, even when the esophagus is divided in the least vascular of its cervical part.

Before beginning the resection of varying lengths of the esophagus we decided to try division of the least vascular part of its thoracic portion, that is, the 2 to 3 cm. adjacent to the diaphragm. Three operations were performed, and the results obtained show that this method of suture

Fig. 4.—Lower end of the thoracic part of the esophagus removed 107 days after operation, showing healed line of suture.

ensured a blood supply to the line of anastomosis sufficient to avoid sloughing even in this scantily supplied portion of the esophagus. Empyema occurred in two animals, but the line of suture in each instance remained intact. One operation was successful in every respect (fig. 4).

The results following the use of this method of suture for end-to-end anastomosis of the divided esophagus were encouraging enough to warrant the investigation of its efficacy after resection of varying lengths

of the organ, when considerably more tension would be put on the line of suture than after simple division.

In only one of the four operations in which the esophagus was resected in the cervical portion did sloughing of the line of suture occur with ensuing fatal infection, although this was localized and had not extended into the mediastinum. The other three operations were entirely successful. A slight degree of stenosis found at necropsy in two of the animals was purely anatomic, and, judging from the good health of the animals up to the time of necropsy, it did not have any functional signifi-

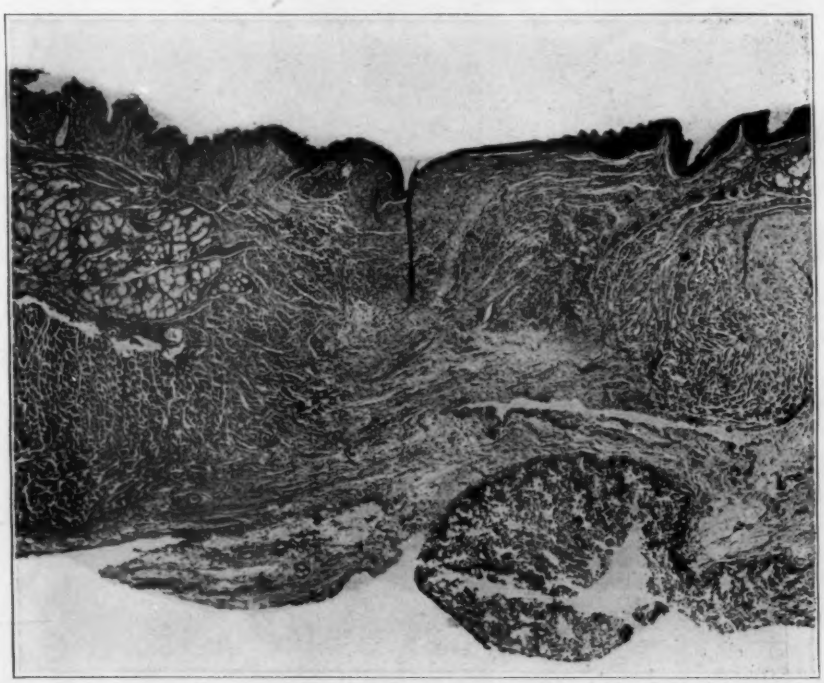

Fig. 5.—Specimen distended with water, removed 145 days after operation. A slight decrease in size of the lumen has occurred.

cance as they ingested their food in a perfectly normal manner. A maximal length of 4 cm. of the cervical part of the esophagus was resected successfully (figs. 5, 6, 7 and 8).

Three of five animals in which resection of the thoracic part of the esophagus was performed survived in each case with a perfect functional result (fig. 9). In only one case did the line of anastomosis slough with a fatal result. The other death was due to hemorrhage, and its most likely source seems to have been the intercostal artery posteriorly near the vertebral column. On a few occasions complete hemostasis in this

area was difficult to obtain. One of the animals is under observation and appears to be normal 301 days after operation (Jan. 1, 1929).

Four centimeters of esophagus was successfully resected. This was approximately one seventh of the total length. In certain portions of

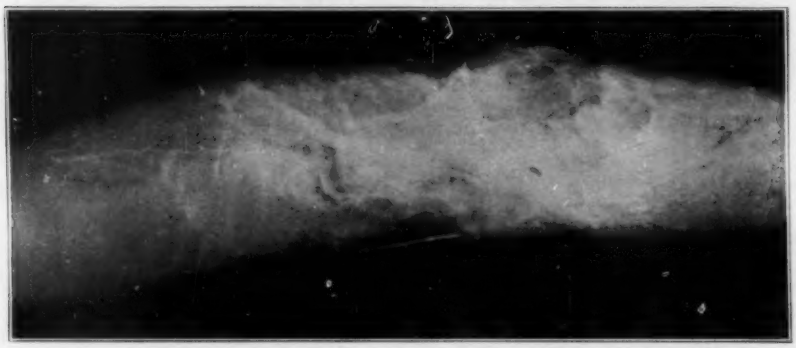

Fig. 6.—Mucosal surface of specimen shown in figure 5. The thinned raised ridge which marks the site of section appears greater than it really is, as shown in figures 7 and 8.

Fig. 7.—Longitudinal section through line of anastomosis of specimen removed 145 days after operation. The line of anastomosis is hardly discernible; × 100.

the esophagus it would seem entirely feasible to resect a longer segment successfully. It should be noted that the results reviewed included all the operations performed by this technic. Most of the unsuccessful operations occurred during the development of the method and were due

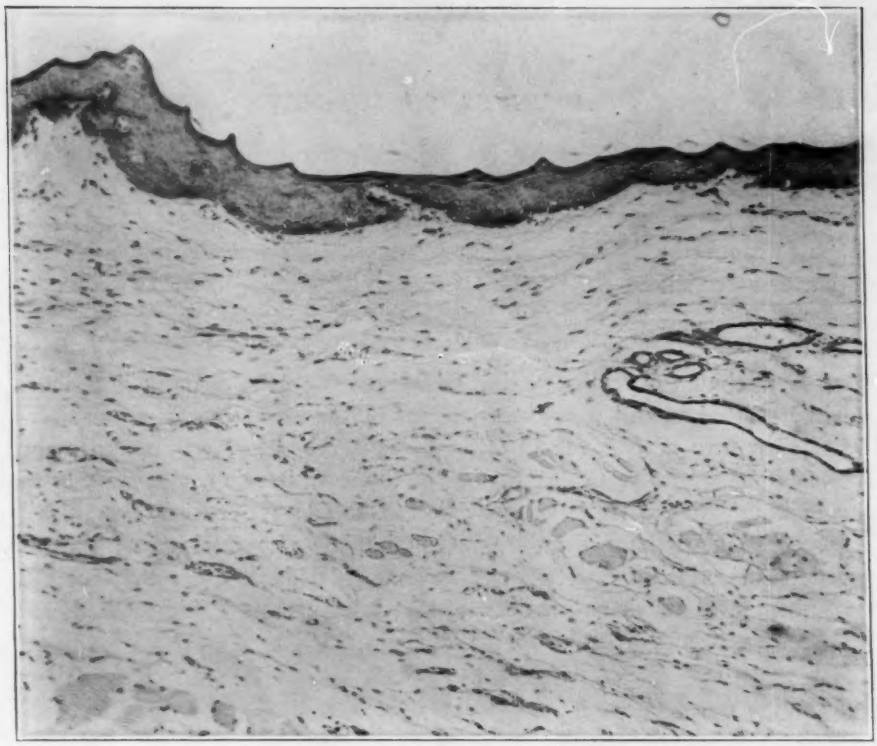

Fig. 8.—A higher magnification of a portion of the section shown in figure 7; × 500.

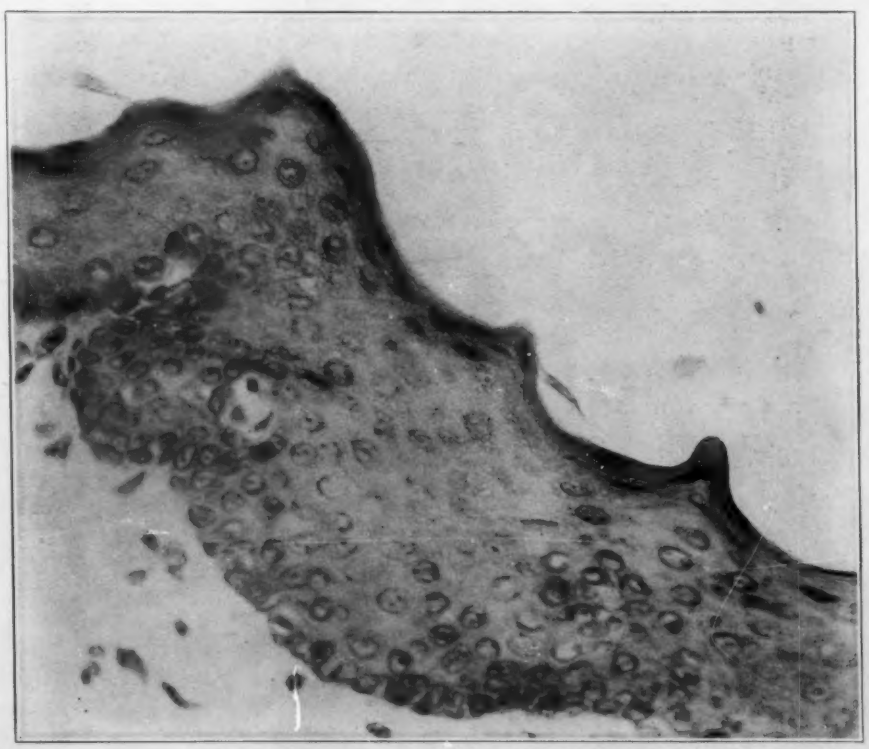

Fig. 9.—Longitudinal section through line of anastomosis of specimen removed seventy-nine days after operation. Almost complete repair has occurred; × 12.

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to faults which were later corrected. We are confident that once the technic is developed a high percentage of success can be obtained. Whether or not any portion of the technic can be adapted to human beings cannot be determined at present. Experimentally, however, section or resection of the esophagus can be accomplished successfully.

SUMMARY

A method for section and resection of the esophagus is described. The essential special procedures are: (1) the employment of an interrupted suture of fine silk in order to conserve the blood supply to the line of anastomosis; (2) sectioning of the left phrenic nerve in order to help immobilize the site of operation, and (3) preventing the animal from taking anything by mouth, and maintaining its nutrition with intravenous injection of dextrose and sodium chloride in order to place the esophagus, as much as possible, at physiologic rest. This method has proved successful in experimental surgery.

CONGENITAL ATRESIA OF THE BILE DUCTS

ITS DIAGNOSIS AND A CONSIDERATION OF SURGICAL INTERVENTION ON THE BASIS OF ITS PATHOLOGY *

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Though a relatively large number of cases of congenital atresia of the bile ducts has been reported, attention has been restricted for the most part to the academic, if interesting, discussion of the anomaly at autopsy and to the possible etiologic factors involved. Little has been written on the management of these cases. Little has been said in reference to the worth of therapeutic procedure and the indication for surgical intervention. We report a case in which attention is focused on the problem of what to do for the child. We present the difficulties which confronted us in establishing our diagnosis and the perplexities which troubled us in planning our therapy. We shall, therefore, discuss in some detail the problems of differential diagnosis, but more especially do we wish to take up the question of the wisdom of surgical intervention on the basis of the underlying pathologic changes.

REPORT OF A CASE

History.—A. R., a white girl, aged 3 months, was admitted to the Pediatric Service of the Brooklyn Hospital on Feb. 14, 1928, the chief complaints being cough and fever of three days' duration and jaundice and white stools since birth. From birth to the time of admission, the mother had noticed an increase in the depth of the jaundice. The patient was the sixth child in the family, a full-term infant, delivered by a midwife, with an ambulance physician in attendance. The labor was easy and of short duration. It was noted at birth that the skin and sclerae were yellow. Otherwise, the child seemed normal. There was no desquamation of the palms or soles, no fissuring and no snuffles.

The child was given the usual care for the new-born infant, but developed an umbilical infection which persisted for two months, during which time there was a profuse yellow purulent discharge from the stump. There was apparently no fever. The child was put on three hour breast feedings and apparently gained weight, although vomiting occurred occasionally during the second and third months. The mother noticed that the stools were always either white or light gray and rarely faintly yellow. There were about three or four a day; they were well formed, without curds and with no apparent increase in bulk. There was no foul odor. The urine was persistently dark brown.

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* From the Pediatric Service of the Brooklyn Hospital (service of Dr. A. D. Smith).

Three days before admission, on Feb. 11, 1928, the child had some fever, cough and anorexia, and was taken to the Children's Clinic for treatment. The family history was essentially negative, with no history of miscarriages or stillbirths. Both the father and the mother were well. Five other children, all boys, were living and well. The Wassermann reaction of the blood of the father was 3 plus; that of the mother was negative on two occasions. The Wassermann reactions of the blood of the five children were all negative.

Examination.—On examination, the patient showed an intense uniform jaundice. The pharynx was injected. There were many medium and fine moist râles throughout both lungs, without any definite signs of consolidation. The abdomen was slightly distended. The liver dulness in the midclavicular line extended from the fifth rib above to 6.25 cm. below the costal margin, and in the axillary line to the anterosuperior spine. Its surface was hard but apparently not irregular, and the child manifested no apparent discomfort when it was palpated. The spleen was palpable 3.5 cm. below the costal margin. It was smooth and firm, but not tender. The observations in the physical examination were otherwise negative.

The temperature was 102 F., the pulse rate 110 and the respirations 35. The white blood cell count was 23,400, with 70 per cent polymorphonuclears and 30 per cent lymphocytes. The hemoglobin content was 72 per cent. The urine was dark brown, with a faint trace of albumin and a markedly positive reaction for bile. The Wassermann reaction of the blood was negative on two occasions. Daily examinations of the stools showed a slight trace of bile by Gmelin's test on two occasions; at all other times the reaction for bile was negative. The fragility of the red blood cells began at 0.4 per cent and was complete at 0.325 per cent. The coagulation time was six and a half minutes; the bleeding time, two minutes. The results of the intradermal tuberculin test, 0.1 mg., were negative. Roentgen examination of the chest showed increased density at each hilum with increased infiltration in the right lower lobe and patches of density well out in the axillary line just above the diaphragm.

Treatment and Course.—The patient was put on routine treatment for pneumonia in infants—mustard plasters to the chest every four hours, tincture of digitalis, forced fluids and feedings of 3 ounces (89 cc.) of 50 per cent skimmed milk (boiled skimmed milk and boiled water, equal parts) every three hours, supplemented by breast milk from the mother when obtainable.

On February 15, the temperature returned to normal. The patient seemed much better and took all the feedings well. A somewhat bothersome cough persisted.

On February 17, examination of the chest showed a few scattered râles at both bases but no dulness. The breath sounds were harsh but distinctly vesicular.

On February 21, the signs in the chest, previously described, were no longer present. The drum of the right ear ruptured spontaneously, liberating a small amount of bloody serum.

Influenced in part by the positive Wassermann reaction of the blood of the father and in greater measure by repeated urgings to try antisyphilitic treatment, we instituted, against our better judgment, a course of such therapy, even though no stigmas of syphilis were present and the Wassermann reaction of the blood had been negative on two occasions.

On February 26, 0.03 Gm. of sulpharsphenamine was given intramuscularly with no untoward reaction, and doses of 0.04 and 0.05 Gm. were given on March 3 and 12, respectively, with no harmful results.

On March 15, the child was discharged to the outpatient department for continuation there of antisyphilitic treatment and follow-up. The respiratory symptoms had cleared entirely. The jaundice was of the same intensity. The liver and spleen were about the same size as at the time of admission.

On March 26, the patient was seen in the outpatient department. Her condition was little changed; the jaundice was of the same intensity; the temperature was 100.4 F. She had gained 10 ounces (283.5 Gm.) since the previous visit.

On April 7, 0.5 grain (0.03 Gm.) of mercuric salicylate was given intramuscularly. This was followed in a few hours by fever and vomiting. The child appeared quite ill and the mother reported that she thought that the jaundice had deepened. Abdominal distention occurred, but after about forty-eight hours the apparent ill effects of the injection had disappeared.

On April 14, the intramuscular injection of 0.5 grain of mercuric salicylate was followed by a repetition of the illness observed subsequent to the injection of mercury of the previous week, namely, anorexia, malaise, vomiting, fever, abdominal distention and increase in the depth of the jaundice. Some bright red blood tinged the stools, but at no time were they dark or tarry. The antisyphilitic treatment was discontinued.

On April 18, the child was again seen in the outpatient department. She had lost 6 ounces (170 Gm.) since March 26, and the general condition seemed so much worse that admission to the hospital was advised.

On admission, it appeared that the general nutrition of the child had evidently suffered since the time of discharge, almost five weeks before. The jaundice was possibly a little deeper than at that time. The gums were somewhat swollen and reddened. The heart and lungs were normal. There was moderate abdominal distention. The liver was now 10 cm. below the costal margin in the midclavicular line, and the spleen 6 cm. below the costal margin. Both organs were hard, not tender, and apparently smooth. The temperature was 102 F.

The child was put on a skimmed milk diet, 6 ounces (178 cc.) of the following being given every three hours:

Skimmed milk	24 ounces	(710 cc.)
Dextrimaltose, no. 1	1 ounce	(30 cc.)
Water to make	36 ounces	(1,065 cc.)

The urine was dark amber, but was negative for albumin, sugar and acetone; bile was definitely present. Colonic irrigations were necessary to control the distention.

On April 20, the temperature returned to normal and remained so for three days. The general condition of the child seemed much better. The size of the liver and spleen and the depth of the jaundice were unchanged.

On April 23, all the feedings were taken poorly. Abdominal distention was still a disturbing feature.

On April 25, the temperature rose to 102.5 F., but despite this the child's general condition seemed somewhat better and the distention was less. Nothing definite could be found to account for the rise in temperature.

On April 27, the temperature remained elevated, although there was no demonstrable cause. At 6 p. m., a large amount of curdy material was vomited. At 10 p. m. and at 2 a. m., the child took her feedings well, but she vomited a slight amount of the 2 a. m. feeding. The respirations rose to 50 per minute. At 2:30 a. m., the child became cyanotic, and there was marked abdominal distention which was somewhat relieved by colonic irrigation. The infant's condition did

not seem immediately grave, but at 3:30 a. m., after vomiting bloody material, she became cyanotic and died rather suddenly.

Autopsy.—The body was that of a poorly nourished girl of about 5 months of age. The skin was deeply jaundiced and dark greenish yellow. The abdomen was enlarged and prominent. On ventral incision, the subcutaneous tissues appeared deeply jaundiced. The parietal peritoneum and pleura were deeply icteric.

The lungs were of normal appearance, were light pinkish red and contained air in all parts. The cut section was normal.

The heart was normal in size and shape. The intimal surfaces of the aortic and pulmonary valves were deeply bile-stained. The heart was otherwise normal.

The liver was large, weighing 175 Gm., of normal shape and dark greenish brown. It was hard and the surface was finely pebbled. On section, it cut with increased resistance. The cut surface was dark greenish brown. The gallbladder was present as a slender, elongated structure in a deep but narrow gallbladder fossa. The lumen of the gallbladder was readily found. It contained no bile and the walls were thin; the inner surface was pale yellowish white. The portal vein and hepatic artery were readily found in the edge of the gastrohepatic omentum, but no structure identifiable as a common bile duct could be found. It appeared to have been absent congenitally. The cystic duct was traceable a short distance from the neck of the gallbladder, but appeared to end blindly in a fibrous strand in the gastrohepatic omentum.

The intestines were moderately dilated with gas and fluid contents; the mucosa was deeply jaundiced. Section down the duodenum showed no structure with the appearance of a papilla of the bile duct.

The spleen was large and extremely firm, weighing 75 Gm. The capsule was normal. On section, the cut surface was dark brownish red; no follicles were visible.

The kidneys were of normal size and shape, slightly firmer than normal and so deeply jaundiced that the renal markings were greatly obscured.

The anatomic diagnosis was: congenital atresia of the bile ducts; splenomegaly, and icterus, general.

Histology.—Microscopic preparations from the liver showed marked periportal fibrosis, obviously of long standing. The bile radicles of all sizes were filled with thick pellets of bile. Sections through the gastrohepatic omentum showed the portal vessels and disconnected islets of epithelium of the hepatic and common bile ducts, but no epithelial lined lumen was demonstrable. The incorporation of bile pigment by Kupffer's cells was practically absent.

Sections of the spleen showed that the increase in size was mainly due to thickening of the walls of the venous sinuses, distention of the venous channels and increase in the size of the endothelial cells which lined the sinuses. The endothelial cells of the sinuses and the large clear cells of the splenic follicles contained black pigment in the form of coarse granules and globules.

The epithelium of the kidney was granular, and the jaundice that was so obvious grossly was practically imperceptible histologically. The changes in the kidney appeared to be confined strictly to the tubule cells which were enlarged and granular.

Examination of the epiphyseal and diaphyseal lines of the long bones showed no evidence of syphilis. There was no osteochondritis.

Fig. 1.—The liver and spleen, showing the relative sizes. The slender and collapsed gallbladder should be noted.

Fig. 2.—Section through the liver, showing dilated radicles of the gall duct filled with bile. The mottling due to cirrhosis should be noted.

Fig. 3.—Section through the liver, showing the solid cord containing the hepatic vessels. Note the absence of radicles of the gall duct at this level, taken 1 cm. below that shown in figure 2.

COMMENT

Though there was little doubt clinically that the jaundice was due to a congenital atresia of the bile ducts, there were several disturbing factors which required consideration. First, the history of a chronic infection of the umbilicus for two months suggested an infectious basis for the condition and, secondly, the presence of a 3 plus Wassermann reaction in the father pointed to syphilis as a likely cause.

The absence of a rise in temperature or other signs of sepsis in the general appearance of the infant and the duration of the jaundice spoke strongly against a septic condition. Syphilis, we believed, could be excluded with a fair degree of certainty in view of the absence of any syphilitic stigmas and of a response to antisyphilitic therapy.

One other cause of contention was the presence on two occasions of traces of bile in the stools. These were specimens of enemas, uncontaminated by urine, that gave rise to speculation as to the presence of complete as against incomplete atresia or stenosis. It was postulated then, and evidently correctly, that a deeply stained intestinal mucosa might possibly ooze bile into the lumen of the intestinal tract, or that desquamation of sufficient bile-stained epithelial cells might occur to stain the fecal contents, even though complete atresia was present. The deeply stained mucosa disclosed at autopsy made it appear certain that this was the mechanism for the appearance of bile in the stools.

From a clinical standpoint, the general well-being of the child, despite the complete shutting off of bile from the intestine and the resulting intense jaundice, is most interesting. Although vomiting occurred occasionally, the nutrition was generally well maintained and the child gained surely, if slowly.

How long, then, may life go on in the presence of complete obstructive jaundice?

Lavenson [1] reported a series of sixty-two cases, in which only three patients lived longer than three months, two for nine months and one for eleven months. The majority of patients lived more than four weeks. Several unprecedented cases of long life have been reported, but these apparently did not occur in instances in which complete atresia of a congenital nature was present. Treves [2] reported a case of obstructive jaundice of sixteen years' duration, coming on at the age of 3 years; he operated on the patient at the age of 19. At operation, the cystic and the hepatic ducts were normal and joined to form a common duct which ended almost at once in a hard fibrous nodule which was placed transversely to the long axis of the duct. The

1. Lavenson: J. M. Research **13**:61, 1908.

2. Treves: A Case of Jaundice of Sixteen Years' Standing Treated by Operation, Practitioner **62**:18, 1899.

common duct was one-half inch (1.27 cm.) in length. It was impervious at its distal extremity and ended abruptly at the fibrous nodule, beyond which no trace of a duct could be discovered nor was any duct noted entering the duodenum.

As an explanation for the lengthy survival in this case, Wangensteen [3] offered the explanation that the obstruction was produced slowly, thus affording time for replacement of connective tissue and preventing rapid destruction of liver cells which, rather than retention of the toxic constituents of the bile in the blood and tissues, he postulated to be the cause of toxemia and death.

PATHOGENESIS

We shall not attempt to review the much debated question of pathogenesis. Much has been written on this subject. Thomson,[4] Rolleston and Hayne,[5] Lavenson [1] and others propounded theories to account for the occurrence of atresia. Much difference of opinion still exists as to whether the condition is congenital in the sense of an anomaly of development or whether an inflammatory process is at the basis of it. Holmes,[6] and Howard and Wolbach [7] reviewed thoroughly the conflicting theories thus far presented. The problem deals with embryologic development of which there is no exact knowledge, and it is probable that we are still a long way from understanding the precise mechanism of the causation of obliteration.

PATHOLOGIC ANATOMY

Holmes [6] depicted graphically the anatomic condition present in the cases reported up to his time. The cystic duct, the hepatic duct and the gallbladder may or may not be present. In many cases only a vestige of these structures is found. There is, of course, no passageway for bile to enter the duodenum. The liver is usually increased in size, although atrophy has been noted. It is leathery, tough and firm; the surface is irregular, granular and usually dark green. The cut surface reveals an increased amount of connective tissue. The spleen is often enlarged. Aside from the jaundice, which is general, there is nothing noteworthy in the other organs.

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3. Wangensteen, O. H.: How Long May Man Live with Obstructive Jaundice? J. A. M. A. **90**:1683 (May 26) 1928.

4. Thomson, John: On Congenital Obliteration of the Bile Ducts, Edinburgh M. J. **37**:523, 1891.

5. Rolleston and Hayne: Brit. M. J. **1**:758, 1901.

6. Holmes, J. B.: Congenital Obliteration of the Bile Ducts, Am. J. Dis. Child. **11**:405 (June) 1916.

7. Howard, C. P., and Wolbach, S. B.: Congenital Obliteration of the Bile Ducts, Arch. Int. Med. **8**:557 (Nov.) 1911.

HISTOLOGY

Histologically, a biliary type of cirrhosis is present. The bile capillaries are usually filled with dark brown thickened bile. There is a marked increase in connective tissue which replaces the liver cells in many of the lobules.

The study of the spleen in our case appears to afford what is, perhaps, another explanation for the enlargement of that organ in connection with cirrhosis of the liver. Microscopically, there is an increase in the size and number of the endothelial cells which line the venous loops and sinusoids. These cells are filled with a dark pigment, suggesting that the endothelial system of the spleen has taken up the function of the liver in removing these substances, which are undoubtedly related to the cholemia. This endothelial cell hypertrophy and proliferation, more than the accompanying venous stasis resultant on the cirrhosis of the liver, appears to account for the enlargement of the spleen.

DIFFERENTIAL DIAGNOSIS

Icterus Neonatorum.—This benign, almost physiologic type of jaundice has been variously reported in from 30 to 80 per cent of all newborn infants. Definite recession usually occurs, even in the severe cases, by the end of the second week, although in exceptional cases it has been known to last as long as five weeks. Bile is present in the stools. There should be no difficulty in differentiating this condition from that due to complete atresia of the bile duct.

Icterus Gravis Neonatorum.—This rare condition is usually fatal in the first few weeks of life. The cases in which the patients survive for a longer period may be differentiated from congenital atresia of the bile ducts by the presence of bile pigment in the stools. The disease, too, is often associated with cerebral manifestations—irritability, hyperesthesia, crying attacks, spasticity of the extremities and sometimes of the muscles of the trunk.

Chronic Interstitial Hepatitis.—From interstitial hepatitis, the differential diagnosis is often most difficult. In the early weeks of life, the diagnosis may well be in doubt. Munns'[8] case clinically so closely resembled atresia of the bile ducts that it was diagnosed as such during life. His patient developed jaundice at the age of 18 days; the stools at first were yellow and two days later became clay colored. The infant continued to gain weight steadily while under observation the first few months of life, and the general condition seemed good. At about 4½ months, examination revealed a small, markedly jaundiced, poorly nourished male infant, not acutely ill. There was some evidence

8. Munns, G. F.: Chronic Interstitial Hepatis, Am. J. Dis. Child. **31**:469 (April) 1926.

of rickets. The liver was 4 cm. below the costal margin. The spleen was enlarged. The stools were acholic. The Wassermann reaction of the blood was negative. The van den Bergh test gave the indirect reaction. The stools continued to be acholic for the most part, but were occasionally yellow. The child continued to do remarkably well during the first year, despite the jaundice. At 14 months, examination revealed an undernourished, markedly jaundiced infant who could sit alone but could not stand. The abdomen was distended and the liver reached to the umbilicus. Operation was advised but refused. The jaundice progressed; ascites developed, requiring paracentesis, and 450 cc. of straw-colored fluid was removed. The van den Bergh test gave the direct reaction in blood and ascitic fluid. The stools, however, varied from yellow to brown and there were from one to three movements daily. The anemia became progressive. Fluid continued to reaccumulate in the abdomen, and paracentesis was necessary twice. The child continued to grow worse. The temperature rose gradually to 103.8 F. Signs of congestion were present in the lungs, and death ensued at the age of 15½ months.

Autopsy revealed that the ampulla of Vater and the common, hepatic and cystic ducts were patent. The common bile duct averaged from 3 to 6 mm. in circumference. The gallbladder was adherent to the mesocolon and the colon by firm fibrous adhesions. The liver was firm and dark olive green; the capsule was thin and transparent and the surface smooth. The spleen was slightly enlarged. The pancreas was normal.

Microscopic section of the liver showed an extensive chronic interstitial hepatitis. There was an abundance of brown pigment in the large epithelial cells.

Syphilitic Hepatitis.—This disease presents difficulties similar to those encountered in chronic interstitial hepatitis. Indeed, the case described under chronic interstitial hepatitis is in all respects similar to the clinical picture manifested by syphilitic hepatitis. In most cases, however, the presence of other stigmas of syphilis, the family history and the parental and the patient's serology in the blood or spinal fluid are of the greatest aid.

Icterus of Septicemia.—Differentiation from the jaundice of sepsis is usually made by the character of the temperature, the toxemia, the local umbilical infection often present, the presence often of a bacteremia, hemorrhages from the cord, bleeding into the skin and mucous membranes and the usual rapidity of the course in a septic condition.

Cholelithiasis.—Though this condition in infancy is extremely rare, cases have been observed. Still[9] remarked that cases are "commoner

9. Still: Common Disorders of Childhood, ed. 3, New York, Oxford University Press, 1920, p. 304.

in infancy than at any other period of childhood." Of twenty-three cases described by this writer, "fifteen were in infants and fourteen of these were infants under 10 months of age. In several of these there was intense jaundice at birth or shortly afterwards, and calculi were found in the ducts. In one of my own cases minute calculi were found impacted in the common duct in an infant aged 9 months, but there had been no jaundice."

Acute Catarrhal Jaundice.—As rare as congenital atresia is, acute catarrhal jaundice in the first few weeks of life is probably rarer. Cases do appear in the literature from time to time, and it is important that one know its manifestations in considering jaundice in infancy. Henoch [10] observed one case in an infant at the age of 8 weeks and another at 5 months. Flesch [11] reported one case in an infant under 1 year in 160,000 admissions to the Stefanie Children's Hospital in Budapest; his patient was 1 month old. Skormin [12] reported three cases in infants—one at 1 month, one at 14 days and one at 4 days—who died. Postmortem examinations showed duodenitis with hemorrhage into the brain and meninges. The infant, aged 14 days, died, and a colon bacillus and a few cocci were cultivated from the blood and liver. No hepatitis was present. In view of the course and the observations at autopsy in these two cases, it is questionable whether they were primarily instances of acute catarrhal jaundice. In a series of 430 cases of acute catarrhal jaundice reported by Neumann [13] in Berlin, six were in the first year of life, one each at the age of 56 days, 2½ months, 4 months, 8 months and 9 months. Of Langer's [14] 144 cases, only one occurred during the first year of life. In recent years, Hempelman [15] reported three cases in infants—one, aged 8 months, one, 11½ months, and another, 2 months. In all his cases, the duration of the jaundice was short; in the first, six days; in the second, from about a week to ten days, and in the third, about two weeks.

The differential diagnosis of congenital atresia of the bile ducts from acute catarrhal jaundice should never be difficult. The short

10. Henoch: Vorlesungen über Kinderkrankheiten, Berlin, A. Hirschwald, 1897, p. 571.

11. Flesch, H.: Beitrag zum Icterus infectiosus epidemicus im Kindesalter, Jahrb. f. Kinderh. **60**:776, 1904.

12. Skormin, B.: Ueber die verschiedenen Formen des Icterus im Säuglingsalter, Jahrb. f. Kinderh. **56**:176, 1902.

13. Neumann, H.: Bemerkungen über die gewöhnliche Gelbsucht und ihr Vorkommen in Berlin, Deutsche med. Wchnschr. **35**:574, 1899.

14. Langer, J.: Ueber gehäufteres Auftreten von Icterus catarrhalis bei Kindern in Prag und dessen Umgebung, Prag. med. Wchnschr. **30**:319, 1905.

15. Hempelman, T. C.: Catarrhal Jaundice in Infancy, Am. J. Dis. Child. **10**:39 (July) 1915.

duration of catarrhal jaundice at once distinguishes it from malignant atresia.

TREATMENT

Porter,[16] writing in Abt's Pediatrics, remarked "there is no treatment that can be undertaken with any hope of success." Yet, from an anatomic standpoint, it would seem that if surgical intervention could effect the opening of a channel for bile to reach the intestine, a cure ought to be effected. But why has surgical intervention thus far failed to hold out the hope expected of it?

First, in only 16 per cent of the reported cases has operation been anatomically possible; i.e., sufficient structure was present to allow the creation of a passageway for bile to reach the intestinal tract. Secondly, the degree of hepatitis may be extremely marked and the radicles of the intrahepatic bile ducts so obstructed that what appears to be an adequate external outlet for the bile does not at all solve the problem.

Parsons and Hickmanns[17] reported the case of a patient with biliary cirrhosis with atresia of the extrahepatic bile ducts. Their patient developed a severe, continuous jaundice at the age of 3 weeks, which persisted until death at 6 months. The infant was full-term, breast fed for two weeks and fed thereafter on milk prepared by a formula only. With the onset of the jaundice, the urine became dark and the stools clay colored. On admission, the child appeared well nourished and weighed 8 pounds and 10 ounces (3.9 Kg.). The liver was enlarged, firm and reached almost to the umbilicus. The spleen was not felt. The Wassermann reaction of the blood was negative. In the course of the illness, the jaundice varied slightly in degree, though a fortnight before death it was less marked than it had ever been. Vomiting occurred only once. The infant lost weight gradually and died rather suddenly about sixteen weeks after admission. The weight at the end was 7 pounds and 6 ounces (3.38 Kg.).

They noted:

> . . . we feel that this case lends little support to the view that the cirrhosis follows on a developmental defect of the bile ducts, but suggests that whatever may be the cause of the condition, it is one which attacks the liver parenchyma at as early a stage as the bile ducts and offers definite evidence that the whole process may be an intra-hepatic one. If this view is correct, surgical intervention, at any time after the diagnosis is made, cannot offer any chance of complete recovery, because a marked cirrhosis of the liver must be present. In this patient, surgical treatment would obviously have been quite useless.

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16. Porter, Langley; in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 646.

17. Parsons, L. G., and Hickmanns, E. M.: Biliary Cirrhosis, Am. J. Dis. Child. **31**:459 (April) 1926.

Von Reuss,[18] on the other hand, was of the opinion that, "in view of the impossibility of spontaneous recovery, an operation a priori is by no means to be set aside; it should be undertaken, if not during the first few days, in any case as early as possible."

Holmes [6] studied carefully the anatomic anomaly present in the cases reported up to 1916, and observed that in the series of cases in which operation was anatomically possible six of the patients died before the twentieth day of life and nine lived from two to six months. Of the cases in which operations were performed, Giese's [19] was unsuitable. In Oxley's [20] case, only a paracentesis of the tumor was done, with removal of 36 ounces (1.065 cc.) of bile. Theoretically, this was an operable case. Morse and Murphy's [21] case was inoperable, and Putnam's [22] operation was unsuccessful. Treves' [2] case, although successful, leaves great doubt as to the congenital nature of the obstruction.

Until the recent publication of Ladd,[23] we could find no case on record of undisputed congenital atresia of the bile ducts in which operation was successful. This author reported successful operations in six cases of stenosis and atresia of the bile ducts, but of these only the first and third cases were complete congenital atresia, the others being stenosis or obstruction not congenital in origin. It is most hopeful and instructive to know that the first patient, operated on at the age of 3 months, has survived two years; the second patient, operated on at 5 months, has survived seven years. Both were alive when this paper was written.[24]

Though we recognize the courage and skill with which, in these two instances, this seemingly hopeless disease has apparently been mastered, we cannot help but believe that in only the most exceptional cases of congenital atresia of the bile ducts, even though operation is anatomically possible, is it likely that the patient will survive a long period, owing to the cirrhosis of the liver, which is as much a part of the disease as the atresia itself. That exploratory surgical intervention should be tried, we do not deny, but that much can be expected of it, we doubt.

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18. Von Reuss, A. R.: Diseases of the New-Born, New York, William Wood & Company, 1922, p. 272.

19. Giese, O.: Ueber Defect und congenitale Obliteration der Gallenausführungsgänge und der Gallenblase, Jahrb. f. Kinderh. **42**:252, 1896.

20. Oxley, M. G. B.: Congenital Atresia of the Duodenal Opening of the Common Bile Duct in an Infant, Producing a Large Abdominal Tumor, Lancet **30**:988, 1883.

21. Morse and Murphy: Boston M. & S. J. **156**:102, 1907.

22. Putnam, C. P.: Arch. Pediat. **15**:663, 1898.

23. Ladd, W. E.: Congenital Atresia and Stenosis of the Bile Ducts, J. A. M. A. **91**:1082 (Oct. 13) 1928.

24. Ladd, W. E.: Personal communication to the authors.

One does not like to believe that the older surgical procedure should have been so lacking in technic that no patients prior to the one of Ladd should have been reported as cured. Yet there is much to be said for the development in late years of a finer surgical technic in operation on infants. With it has come the recognition that minimal and gentle handling of tissues plus the element of time are essential to a successful outcome. It is to be hoped that the number of recoveries reported will grow with the appreciation of the necessity for special surgical skill during this early period of life. One should never lose sight of the necessity for early operation in these cases, but no caution is too great to make certain of the diagnosis of atresia of the bile duct.

Only recently, one of us had occasion to observe in another clinic a case of a fairly well marked jaundice in an infant, aged 3 weeks, which had come on shortly after birth. The stools occasionally were acholic, but for the most part were faintly yellow. Permission for studying the child's serology could not be obtained, but that of the parents was normal. There was no evidence of syphilis. Hospitalization was refused, the parents being persistent in their opposition to any study of the case. The child was taken regularly to the clinic, and after three months the jaundice had almost entirely disappeared; the child was doing well at the time this paper was written. What overenthusiastic surgical intervention, advocating early operation in cases of protracted jaundice, might have wrought in this frail infant is left to conjecture.

On the basis of our experience in giving antisyphilitic treatment in our case, although no evidence of syphilis was present, we believe that in cases of protracted jaundice in the new-born infant in whom there are no serologic or clinical evidences of the disease, the institution of such antisyphilitic treatment is not advisable. Since vomiting and a general intestinal upset followed the administration of mercury, it is easy to understand that a liver already diseased, as it is in congenital atresia, should not bear too well the burden of added toxic substances, such as mercury or arsenic. The severity of a syphilitic infection which would cause protracted jaundice in a new-born infant as a result of interstitial hepatitis has in all likelihood, already damaged the organism beyond repair. Confirmation of this is found in the general agreement among observers that severe jaundice is not commonly observed in the ordinary type of syphilitic cirrhosis.

CONCLUSIONS

1. In congenital atresia of the bile ducts, in addition to the anatomic obstruction which prevents bile from reaching the intestine, there is marked cirrhosis of the liver which at the time of birth is as much a part of the disease as the atresia itself.

2. The cirrhosis of the liver is so advanced that, even should surgical exploration reveal an apparently operable condition from an anatomic standpoint, the possibility of effecting a cure is not likely.

3. Surgical intervention in cases of protracted jaundice in infancy, diagnosed as congenital atresia of the bile ducts, should be undertaken, but with a full knowledge of the overwhelming odds, both as to anatomic operability and as to the likelihood of affording a cure even when anatomically operable.

4. In cases of protracted severe jaundice in the new-born infant in whom a positive Wassermann reaction and other stigmas of syphilis are absent, a course of antisyphilitic treatment does not appear logical.

5. Traces of bile may be present in the stools of an infant with congenital complete atresia of the bile ducts.

6. The enlargement of the spleen in congenital atresia of the bile ducts appears to be due in great measure to an increase in the size and number of the endothelial cells which line the venous loops and sinuses of the spleen and suggests an attempt on the part of the spleen to asume the phagocytic function of liver cells which have been damaged.

TUMORS OF THE BONE

A COMPARATIVE STUDY *

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In approaching a study of tumors of the bone, one is immediately confronted with a chaos of unsolved problems, pertaining particularly to the osteogenic sarcoma and the giant cell tumor.

Until 1920, when Codman [1] instituted the Registry of Bone Sarcoma, the literature was in a state of confusion because of no satisfactory, workable nomenclature. In this country the writers on this subject are conforming more and more to the classification of bone tumors recommended by the registry committee.

In his able and helpful study of the material of the registry, Kolodny [2] found fault with the classification adopted by the committee and explained his criticism on the grounds that when the classification was made, the material was not so plentiful as now, and that the personnel of the committee consisted chiefly of laboratory men. He recommended the following classification for the primary malignant tumors of the bone, which is not essentially different from the one adopted by the committee:

1. Osteogenic sarcoma.
2. Ewing's sarcoma.
3. Myeloma.
4. Unclassified.
   (*a*) Angio-endothelioma.
   (*b*) Extraperiosteal sarcoma.

As in many diseases in the past, the knowledge of the pathologic anatomy, diagnosis and, to some extent, the treatment for osteogenic sarcoma has advanced beyond the knowledge of the etiology.

Trauma is thought to play an important part in the production of these tumors, and Coley [3] asserted that 50 per cent of the cases present a history of injury so definitely related to the onset of the tumor that it cannot be ignored as a factor. The history of trauma given by the

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1. Codman, E. A.: Surg. Gynec. Obst. **34:** 335 (March) 1922.
2. Kolodny, Anatole: Surg. Gynec. Obst. **44:**1 (April) 1927.
3. Coley, W. B.: J. Bone & Joint Surg. **10:**420 (July) 1928.

patient is frequently not reliable, since it seems to be a part of human nature to try to associate a painful swelling with some injury.

Since osteogenic sarcoma is most prevalent in the young between 10 and 20 years of age who are constantly receiving injuries of various grades of severity, and since the incidence of the disease is quite low, there must be some predisposing factor inherent in the bones so affected. There is much similarity in an active reparative process of growing bone and osteogenic sarcoma. With a loss of growth restraint, this reparative process may eventuate in a malignant tumor. Certainly it seems true that accidental, and even surgical, trauma may cause a malignant change to take place in a benign tumor of the bone.

According to Kolodny, osteogenic sarcoma is understood by the registry committee to mean a sarcomatous tumor derived from the ancestors of cells, which, when duly differentiated, are known as osteoblasts. The adjective osteogenic applied to a sarcoma does not imply that new bone must be produced. In fact, some of the most malignant osteogenic sarcomas form little or no bone. It is true that new bone is usually formed and that at the same time the old bone is being destroyed. Eising [4] described the formation of the perpendicular, fanlike rays of new bone, so characteristic of osteogenic sarcoma, by the stimulating effect produced by the tumor cells on the osteoblasts of the haversian canals. This reactionary formation of new bone follows the vessels outward toward the periosteum. The periosteum also takes an active part in the formation of new bone. Since production of bone signifies differentiation, the tumor containing much bone often pursues a less malignant course than the cellular and vascular growth. Coley thought that the term periosteal sarcoma is a misnomer, since nearly all osteogenic sarcomas start beneath the periosteum proper or have a central origin. He found the classic fanlike radiation shown by the x-ray in only 18 per cent of the cases. Kolodny, in studying the material of the registry, concluded that it was often impossible from the roentgenogram, and even with the gross specimen available, to determine whether the tumor originated from the periosteum or cortex or had a central origin.

There are osteogenic sarcomas the diagnosis of which is quite plain from the clinical and roentgenologic studies. Again, there are tumors which show such variations that the methods of diagnosis, including biopsy and radiotherapy tests, leave one still in doubt as to the true nature of the cases. To err one way may mean the loss of a patient who might have been saved by early radical means. To err the other way may result in an unnecessary, mutilating operation. The average sur-

4. Eising, E. H.: Bone Formation in Osteogenic Sarcoma, Arch. Surg. **12:** 867 (April) 1926.

geon, roentgenologist and pathologist see only a few of these cases, and naturally the doubtful tumors will give great concern as to diagnosis and treatment. Not many of these can avail themselves of the services of the few men who have become expert in this field. It would be helpful for the surgeon to register all of his malignant tumors of the bone and giant cell tumors so that he could study the registry material and at the same time add to the material for the mutual benefit of all interested in the subject. Codman set forth twenty-five criteria which one would do well always to observe in attempting to make a diagnosis of malignant tumors of the bone.

The osteogenic sarcoma which presents the least difficulty of diagnosis will usually be found in a young person, otherwise active and healthy. A good clinical history will usually elicit a complaint of pain, possibly following a trivial injury, and later the appearance of a tumor. The favorite sites for these tumors are the lower end of the femur and the upper end of the tibia. Fifty-two per cent of these tumors are located in the femur. In no instance has an osteogenic sarcoma of the lower end of the tibia or radius been found in the registry material. The clinical appearance of the tumor is somewhat fusiform; the skin is smooth and glazed, and the superficial veins stand out prominently. On palpation the tumor is hard, for the most part, but here and there may be soft or cystic areas. The surface temperature is frequently elevated. The tumor is firmly fixed to the bone and the joint is not involved, but movements of the joint are frequently impaired by the close proximity of the tumor. A roentgenogram will show the newly formed trabeculae of bone and the lipping and elevation of the periosteum up to its firm attachment at the epiphyseal line. The tumor may be seen breaking through the restraining fibrous layer of the periosteum and invading the soft parts. The tumor almost or entirely surrounds the involved bone, but often the shaft will be seen plainly passing through the tumor. In the central and subperiosteal osteogenic sarcomas, the shaft is soon partially or completely destroyed. It is in the latter type of tumor that a pathologic fracture is likely to take place, and since this complication releases the restraint on growth the tumor progresses rapidly and metastases soon follow. One should not be surprised at the absence of the fanlike perpendicular striae of bone because in some of these tumors the bone is laid down parallel to the shaft, and in the large, more slowly growing tumors the x-rays will show a diffuse, irregular spotted appearance of calcification. An osteogenic sarcoma rarely passes through the restraining cartilage; this can be demonstrated on the roentgenogram and after dissection of the gross specimen.

Since the prognosis in osteogenic sarcoma so largely depends on the presence or absence of pulmonary metastases, a roentgenogram of the lungs should always be made. The metastatic tumor may or may not

show formation of bone, depending, according to Eising,[4] on whether or not osteoblasts have been carried to the lungs with the tumor cells.

The first four cases (figs. 1 through 17) of this study were selected because they presented such clear clinical, roentgenologic and microscopic evidence of malignant, typical osteogenic sarcoma of the femur.

During this period of the study, preoperative roentgenologic examination of the lungs was not made as a routine, and it is possible that some or all of these patients had pulmonary metastases before amputation, even though there was no clinical evidence of such lesions. The microscopic sections in each of these four cases showed the characteristic appearance of malignant tumors of the bone, which were diagnosed at that time as osteosarcoma, but which, following the new nomenclature, should be classed with the osteogenic sarcomas. There was no local recurrence or glandular metastasis in any of these patients, but they died within the year following amputation. Three had definite metastases to the lung, and the fourth probably had such metastases.

The fifth and sixth cases (figs. 18, 19, 20 and 21) presented clinical and roentgen evidence as conclusive of osteogenic sarcoma of the femur as that in the first four cases, but biopsies had been done in both cases in other institutions before the patients were admitted to the University Hospital. It has been impossible to secure either slides or tissue from these biopsies, but a diagnosis of malignant disease was reported to the family physician of each patient. In the fifth case, the incision made at biopsy never healed and resulted in a fungating mass. The roentgenogram of the lungs showed metastases. Treatment was refused. In the sixth case, the condition was considered inoperable, and the patient was treated with the mixed toxins of Coley and radiation.

It is in these clearcut, true cases of osteogenic sarcoma, fairly easy of diagnosis, that the prognosis is so poor. The problem of the treatment in these cases is far from being solved. Amputation alone seems to have failed and physicians have turned to radiotherapy, which is still in the experimental stage. Disarticulation or amputation above the proximal joint preceded by radiation locally and to the lungs and followed by radiation and the mixed toxins of Coley seems to me to offer the best chance of arresting the progress of this malignant neoplasm. Cures have been reported following amputation, after radiation and with the mixed toxins and combinations of these. In many of these reported cures there was much doubt as to the malignancy of the tumor. The number of five year cures reported in the literature is too small to create much enthusiasm over any method of treatment.

In sharp contrast to the osteogenic sarcoma is the typical giant cell tumor, which has one-half the incidence of the former neoplasm; it occurs most often in the third decade and is found chiefly in the ends of the long pipe bones, starting in the epiphysis or the extreme end of the

diaphysis but rarely ever involving the joint. The cortex of the bone expands as the tumor grows. Even when the cortex has disappeared the periosteum envelops this tumor, and there is no tendency to invade the soft tissues. If the tumor should break through the periosteum, as sometimes happens after biopsy or pathologic fracture, it does not tend to infiltrate but to grow in the planes of least resistance. The marrow cavity of the shaft is not invaded by the tumor but rather protected by a limiting membrane. As seen on the roentgenogram, the tumor is spherical, trabeculated and multicystic. The shaft of the bone is not present, and there is not the characteristic lipping of the periosteum seen in osteogenic sarcoma. The surface temperature is not usually raised, and superficial veins are rarely dilated. The interior of this tumor has been compared to currant jelly, but in longstanding cases the tumor is more fibrous and solid.

Like osteogenic sarcoma, trauma frequently precedes the appearance of this tumor, but the true etiology has not been discovered.

Codman [5] regarded the giant cell tumor as a benign mass of granulation tissue. Martland [6] thought of it as a phase of osteitis fibrosa cystica. Coley preferred the term giant cell sarcoma, because he found that in certain cases the growth was clinically malignant and death was caused by metastases. He cited six cases in which a diagnosis of giant cell tumor was made, in which the growth proved to be malignant. One of these cases was selected from all the reports of giant cell tumors at the Memorial Hospital and was included by Kolodny in his study of the registry material as showing the most typical example of giant cell tumor. Bloodgood [7] studied 177 cases of giant cell tumor and did not find a single instance of death from metastases.

The histologic structure of the typical giant cell tumor consists chiefly of stroma and giant cells. The stroma is vascular and made up of spindle, round and polygonal cells with vesicular nuclei. The nuclei are not hyperchromatic nor is there much pleomorphism of the cells. The giant cells are opaque, resembling normal osteoclasts with small oval nuclei uniformly shaped and centrally placed.

A good history, physical examination and a roentgenogram will usually lead to a correct diagnosis in the typical case of giant cell tumor. Coley,[3] however, found 20 per cent error in diagnosis based on clinical and roentgenographic evidence alone.

The seventh and eighth cases (figs. 22, 23, 24 and 25) of this report seem to be examples of the typical giant cell tumor. In the seventh case the onset, slow development, pathologic fracture followed by union, roentgenographic appearance and a fourteen year cure after amputation prove the growth to be a benign tumor.

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5. Codman, E. A.: Am. J. Roentgenol. **13**:105 (Feb.) 1925.
6. Martland, H. S.: Proc. New York Path. Soc. **21**:102, 1921.
7. Bloodgood, J. C.: Surg. Gynec. Obst. **38**:784 (June) 1924.

The eighth case is more confusing, but the patient's age, clinical history of a pathologic fracture demonstrated by the roentgenogram and subsequent union after fixation and typical roentgen-ray appearance indicate that the tumor is benign. No doubt the appearance of proliferation of bone and infiltration of the soft tissue was caused by the pathologic fracture. The tumor has responded well to roentgen therapy, as indicated by much sclerosing and thickening of the trabeculae, but sufficient time has not elapsed for the patient to be considered cured. A disadvantage of primary radiotherapy in these tumors is that in case of an error in diagnosis valuable time will be lost in instituting radical treatment. Furthermore, radiotherapy should be directed by an experienced, well equipped radiologist since undertreatment has a stimulating effect on neoplastic growth and overtreatment may cause the tissue to break down, or may produce such brittleness that fractures occur easily, or set up an endarteritis, accompanied by such pain that amputation will have to be done.

Unlike the cellular osteogenic sarcoma, the giant cell tumor increases in size and often becomes more painful for a while after radiotherapy.

Many surgeons prefer to treat the giant cell tumor by curettage and swabbing the cavity with an escharotic. There is 20 per cent of recurrence after this procedure, and there is always danger of infection which will be serious and possibly necessitate amputation, particularly if the joint participates in this infection. Repeated curettage for recurrences may transform the benign tumor into a malignant growth. Stone and Ewing [8] reported a case of giant cell tumor in which the condition was completely altered by repeated curettage. There seems to be some doubt, however, as to the primary benign nature of this tumor.

Meyerding [9] studied twenty-four cases of giant cell tumor of the long bones; fifteen of the patients were treated by curettage, five by amputation, three by resection and one by excision. In five of these, subsequent amputation was performed for recurrences and infection, but in no instance was true malignant disease present.

MacGuire and McWhorter [10] studied twenty cases and found that, following treatment, there was no recurrence in twelve cases; seven of the remaining eight developed local recurrences, in two of which the metastasis occurred to the lungs, in one to the inguinal glands and abdomen and in one massively involved the stump remaining after amputation.

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8. Stone, W. S., and Ewing, J.: Unusual Alteration in Natural History of Giant Cell Tumor of Bone, Arch. Surg. **7**:280 (Sept.) 1923.

9. Meyerding, H. W.: Benign Foreign Body Giant Cell Tumors in Long Bones, J. A. M. A. **83**:1323 (Oct. 25) 1924.

10. MacGuire, C. J., and McWhorter, J. E.: Sarcoma of Bone, Arch. Surg. **9**:545 (Nov.) 1924.

In studying the literature of tumors of the bone, one cannot help but be impressed with the fact that there are various grades of malignancy and many borderline cases in which the diagnosis is difficult. Close cooperation between the surgeon, the roentgenologist and the pathologist is absolutely necessary in the management of these variants. It is in these cases that microscopic examination of tissue removed at biopsy is so essential. When biopsy is done, the surgeon should have permission and should be prepared to do a radical operation in case a malignant condition is found. I see no reason for performing a biopsy on a patient with a hopelessly inoperable osteogenic sarcoma in order to complete the record, since it will certainly increase the rate of growth and will likely cause it to fungate, adding to the misery of the patient till he is relieved by death. If exploration reveals a growth that is suggestive of a giant cell tumor, the whole cavity should be thoroughly curetted and cauterized so that if the pathologist finds the tumor to be benign the proper operative procedure will have been done and the pathologist will have all the tissue for his examination. Too often the pathologist is provided with such meager tissue that it is unfair to expect an intelligent report. The surgeon may or may not follow this curettage with radiotherapy and toxins. Radiation will prevent recurrence but may interfere with sufficient regeneration of bone to give a useful extremity.

Between the true osteogenic sarcomas and the typical giant cell tumors discussed and illustrated in this paper, there are two cases (9 and 10) which seem to me to be borderline or variants. In case 9 the diagnosis at biopsy was osteogenic sarcoma, and amputation was done. This patient was 56 years of age, well beyond the usual age incidence. Seven years before amputation, the clinical and roentgen evidence of a giant cell tumor in the lower end of the tibia was conclusive. The man refused treatment and was not seen until four years later; then, another roentgenogram showed no change in the giant cell tumor, but an erosion on the midportion of the shaft of the tibia was found (case 9 and figs. 26, 27, 28, 29, 30 and 31). Again the patient refused treatment, keeping at his work three years longer and sustaining a pathologic fracture which necessitated his coming to the hospital. The giant cell tumor had increased in size and broken through the capsule. At the site of the tibial erosion a fairly large tumor composed of soft tissue had developed, and a marked contrast was noted between the roentgenogram made three years previously and the one made at this time. The tissue for examination was taken from the tumor on the midshaft. The roentgen-ray films and microscopic slides as well as a clinical record were sent to the chairman and registrar of the Committee on Bone Sarcoma. They have studied this material and concurred in the opinion that this is an atypical case and classified it according to the type of tissue as a mixed cell sarcoma of low grade malignancy. This case is difficult to classify

according to the Bone Sarcoma Registry, there being no classification of mixed cell sarcoma of bone, and the chairman thought that most of the members of the committee would probably classify it as an osteogenic sarcoma.

The tenth case (figs. 32, 33 and 34) is not so confusing as the preceding one, but this patient, too, is beyond the age of highest incidence of osteogenic sarcoma. There was no history of trauma and, as in case 5, pain started in the sole of the foot and in the heel. This pain persisted, creeping up the thigh, for a year before a tumor was discovered. The roentgenogram suggests a giant cell tumor in that there is encapsulation, except where the tumor has broken through in the region of the great trochanter, and definite loculation. New bone, however, extends into the soft tissues and there is destruction of the neck of the femur; the tumor is not sharply defined from the shaft, but destruction of bone seems to be going on at this junction.

The roentgen diagnosis was osteogenic sarcoma, but it seemed wise to do a biopsy in this case. The pathologist made a diagnosis of giant cell tumor but remarked on the possibility of doubt because of the vascular character of the growth, pleomorphism, mitotic figures, true tumor giant cells and tumor ossification.

An amputation at the hip joint was done. The roentgenogram, microscopic slides and a clinical report of this case were also sent to the chairman and registrar of the Committee on Bone Sarcoma; they have classified the tumor as an osteogenic sarcoma, basing their opinion on tumor ossification, although it was of a low type, and on the round and spindle cells showing many mitotic figures and only occasional giant cells.

REPORT OF CASES

CASE 1.—M. L., a white girl, aged 16 years, was admitted to the University of Virginia Hospital on Feb. 10, 1911. Three years before admission, she noticed a small hard mass on the lower posterior aspect of the right thigh. Shortly before this mass appeared she sprained her ankle. The tumor was painless, did not interfere with motion of the joint and grew slowly till about a month before she came for consultation. Pain became severe, and movement of the joint was impaired. Loss of weight was noticed.

On the antero-external aspect of the knee was a scar which was caused by the blade of an axe six years previously. The tumor was fixed; the skin was glazed over it, and the surface veins were prominent (fig. 1).

The roentgenogram (fig. 2) shows a marked periosteal proliferation of the lower 9 inches (22.8 cm.) of the femur, reaching a diameter of about 7 inches (17.7 cm.). There was extensive destruction of the cortex. No abnormalities of the chest were found on clinical examination, and unfortunately the importance of routine roentgen examination of the chest was not realized seventeen years ago. A diagnosis of osteogenic sarcoma was made, and amputation was done through the midthigh (fig. 3). Figure 4 shows an island of cartilage and a blood vessel surrounded by tumor cells. Other sections show bone and areas of spindle cells.

Fig. 1 (case 1).—Osteogenic sarcoma of femur.

Fig. 2 (case 1).—Periosteal proliferation and destruction of cortex.

Fig. 3 (case 1).—Gross specimen showing much formation of new bone and destruction of the outline of the shaft.

Fig. 4 (case 1).—Photomicrograph showing islands of cartilage and blood vessels surrounded by tumor cells.

This patient left the hospital at the end of a month, in fair condition. Her family physician, however, reported that she died of pneumonia shortly after returning home. The "pneumonia" was probably pulmonary metastasis.

CASE 2.—J. W., a white boy, aged 12 years, was admitted to the hospital, Jan. 14, 1915. Two months prior to admission, he fell and wrenched his knee. Pain was not severe enough to confine him to the house and disappeared entirely in a short time. One month later, the thigh began to swell just above the knee, and pain became continuous but not severe enough to interfere much with his sleep.

Fig. 5 (case 2).—Fanlike proliferation and lipping of the periosteum and extensive destruction of bone.

The patient was well nourished and apparently healthy except for the tumor of the femur which extended from the midthigh to the knee joint. The overlying skin was glazed, and dilated veins were conspicuous. There was some elevation of surface temperature. Just above the tumor the thigh measured 32 cm., and the maximum circumference around the tumor was 44 cm. The consistency of the tumor on palpation was described as cartilaginous. There were no enlarged lymphatic glands, nor any clinical evidence of metastasis to the lungs

No roentgenogram of the chest was made. The roentgenogram of the femur (fig. 5) shows a fanlike proliferation of the periosteum, lipping of the periosteum and extensive destruction of bone.

A diagnosis of osteogenic sarcoma of the femur was made, and amputation at the hip joint was done. The gross specimen is shown in figure 6. While the shaft of the bone is much damaged, it still can be plainly seen passing through the tumor. This patient made a satisfactory operative recovery but returned to the hospital two months later in an advanced state of emaciation and with a great deal of dyspnea. A roentgenogram of the chest is shown in figure 7.

Fig. 6 (case 2).—Gross specimen showing shaft of bone passing through the tumor.

The patient died in the hospital two weeks after this admission. Autopsy showed the left lung completely replaced by a tumor which pushed the heart to the right and extended well into the right pleural cavity. On section the tumor presented a honeycombed, hemorrhagic, necrotic appearance with one or two areas of bone formation about 5 cm. in diameter.

CASE 3.—C. R., a white girl, aged 15, was admitted to the hospital on Jan. 5, 1915. About five months before admission, she noticed that she became tired easily and that her left knee was painful on exertion. Three months later, she noticed

Fig. 7 (case 2).—Metastases to the lungs.

Fig. 8 (case 3).—Osteogenic sarcoma of the femur.

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a hard tumor just above and to the inner side of the left knee. The pain gradually became severe and boring. One month before entering the hospital, she fell and hurt her knee and had not walked since. After this trauma, the tumor grew rapidly (fig. 8).

Fig. 9 (case 3).—Osteogenic sarcoma of the femur with proliferation and destruction of bone and pathologic fracture.

The mass was hard, firmly fixed and not tender. The skin was smooth, and the superficial veins were dilated. The surface temperature was raised, and there was fluid in the knee joint. The leukocyte count was 14,000. A diagnosis of osteogenic sarcoma of the femur was made from clinical evidence and roentgen examination (fig. 9). No roentgenogram was made of the chest.

Fig. 10 (case 3).—Gross specimen showing destruction of bone and fracture line surrounded by tumor.

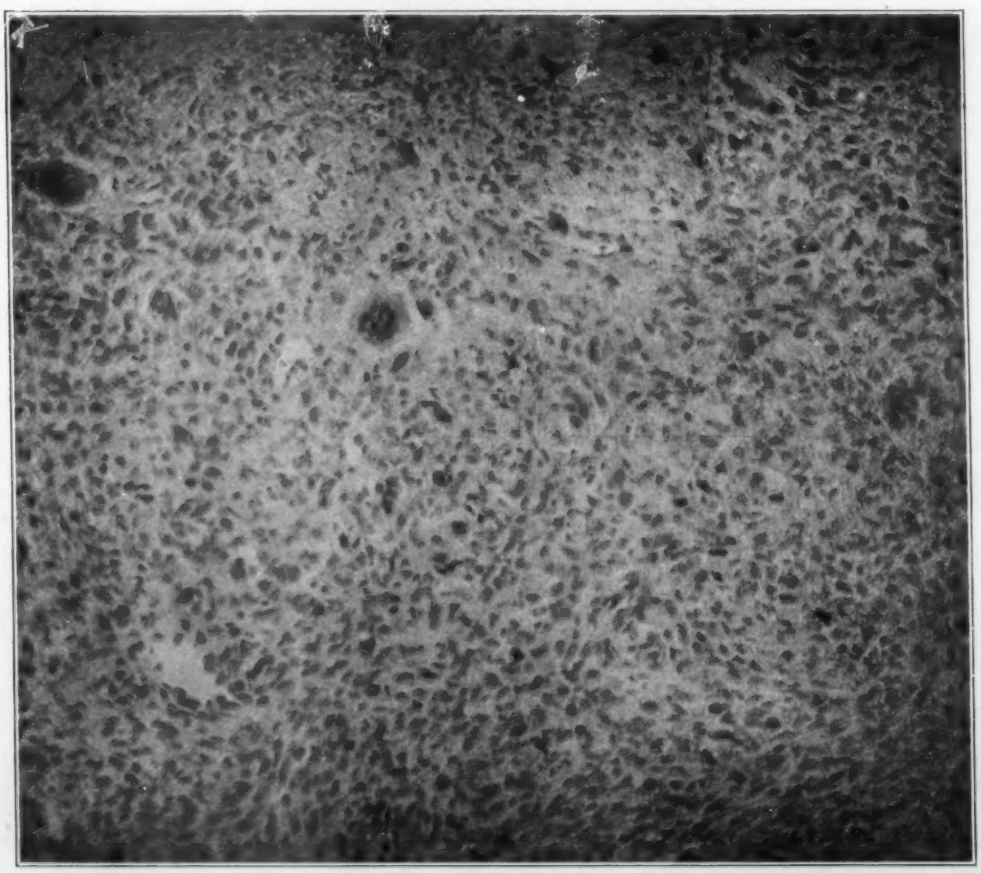

Fig. 11 (case 3).—Photomicrograph showing spindle cells and several giant cells.

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A subtrochanteric amputation was done. The gross specimen is shown in figure 10 and the photomicrographic appearance in figure 11. The stump healed well, and for a while the patient was more comfortable. Signs of metastasis to the lungs developed, and the x-rays showed both lungs infiltrated with tumor (fig. 12). The patient died sixty-five days after admission to the hospital.

CASE 4.—G. H., a white boy, aged 15 years, admitted to the hospital on Feb. 8, 1915, had been a healthy child. One year previous to admission, however, he had pain in his right knee which was diagnosed as rheumatism. Swelling did not appear till six weeks before admission. Two weeks before admission, the patient

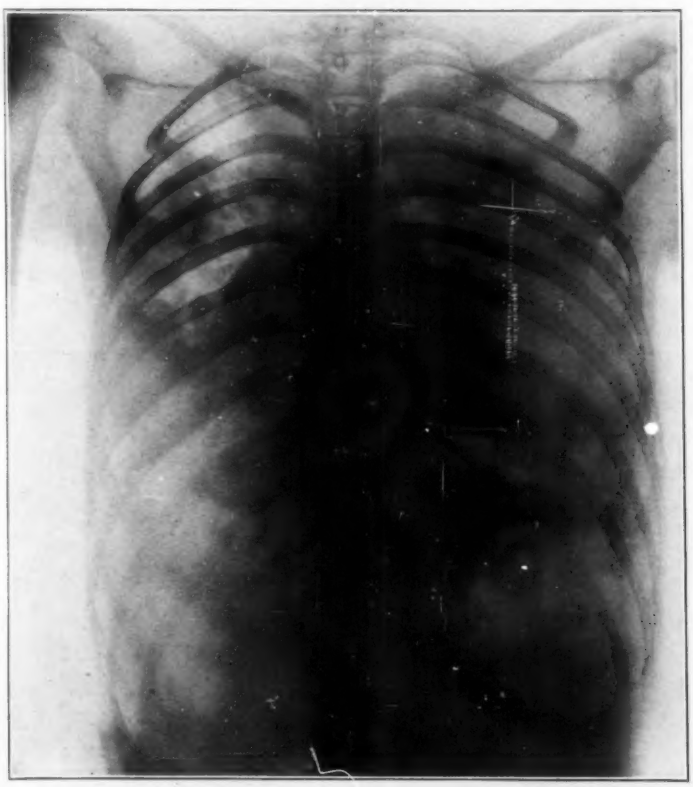

Fig. 12 (case 3).—Extensive metastases to the lungs.

fell on the street and sustained a pathologic fracture. The lower portion of the right thigh was considerably enlarged. The skin was glazed, and the superficial vessels were dilated. The surface temperature was elevated. On the inner aspect of the thigh the tumor was soft, but in other places quite firm (fig. 13).

A diagnosis of osteogenic sarcoma was made from the clinical evidence and x-ray plate of the femur (fig. 14). No roentgen examination of the lungs was made, but the clinical examination revealed no signs of metastasis. An amputation at the hip joint was done. The specimen was sawed open; the medullary cavity of the femur contained a yellowish, granular, cellular growth. This had extended through the cortex of the bone and had produced a pathologic fracture.

Fig. 13 (case 4).—Osteogenic sarcoma of the femur.

Fig. 14 (case 4).—Central bone destruction, elevation, and lipping of the torn periosteum. Also a pathologic fracture.

The gross specimen is shown in figure 15 and the photomicrographic appearance in figure 16.

This patient died with metastasis to the lungs about one year after operation. The roentgenographic appearance of the chest is shown in figure 17.

CASE 5.—C. G., a negro girl, aged 14, was admitted to the hospital on April 18, 1927. Six months prior to admission, she began to have severe pain in the sole of her left foot. Later, severe pain began in the thigh. One month after this onset, she sought medical advice. A diagnosis of malignant disease was made from material removed on exploration. Amputation was advised, but the family of

Fig. 15 (case 4).—Gross specimen showing destruction of bone, invasion and pathologic fracture.

the patient refused. The tumor grew rapidly, and fungus appeared at the site of biopsy.

On admission to the University Hospital, the patient was in a poor state of nutrition. The left thigh was greatly enlarged and was ulcerating (fig. 18). An x-ray film of the left femur (fig. 19A) showed a massive enlargement, with formation of new bone invading the soft parts. The periosteum was visualized along one-half the extent of the femur.

A flat film of the chest (fig. 20) showed numerous areas, rather circumscribed in appearance and varying in size scattered throughout both lungs.

A diagnosis of osteogenic sarcoma of the femur with metastasis to the lungs was made. The patient's condition was considered hopeless, and the family

would not leave her in the hospital since no cure could be promised. She died several months after leaving the hospital.

CASE 6.—B. M., a white woman, aged 22, was admitted to the hospital on May 10, 1924. Nineteen months previous to entering the hospital, she fell from a buggy and bruised her right thigh. Two weeks later, she noticed a swelling on the inner side of the thigh. She was not concerned about this at first, but the tumor grew so fast during the year that she consulted a physician who excised a piece of tissue and gave a diagnosis of malignant tumor of the femur.

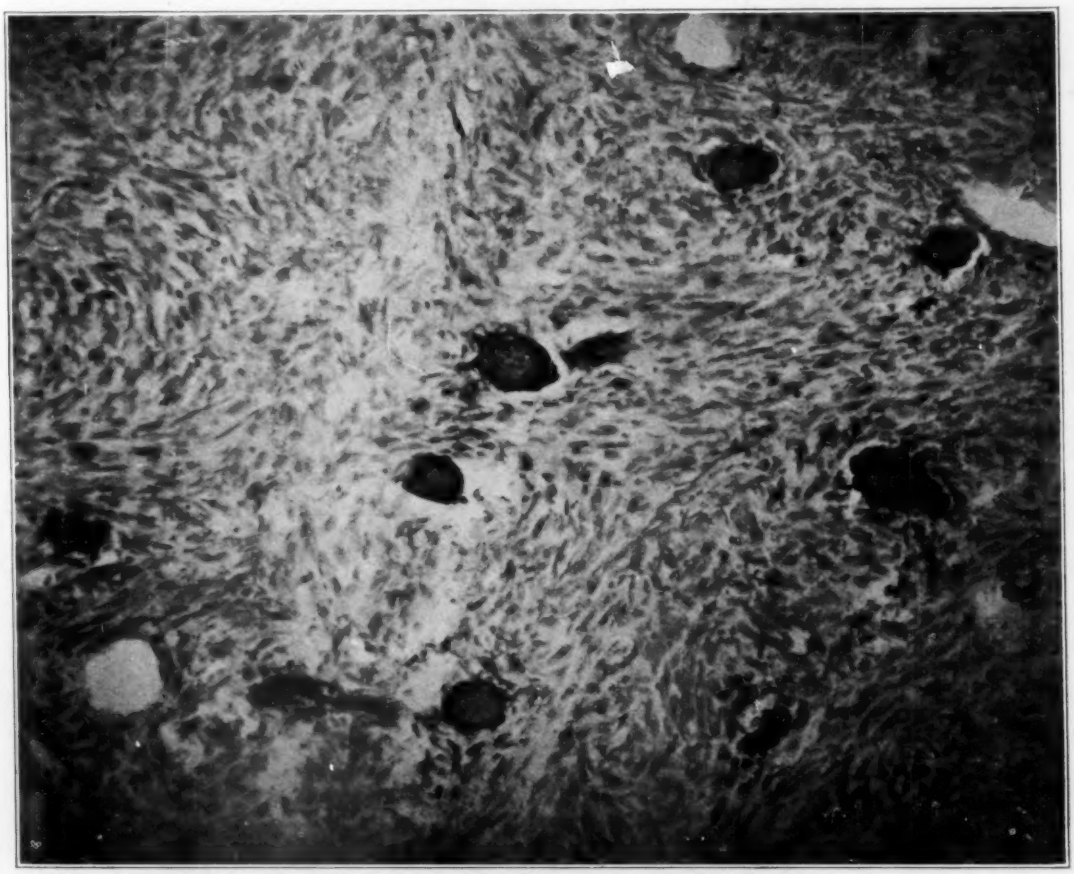

Fig. 16 (case 4).—Photomicrograph showing spindle cells and tumor ossification.

This patient presented an undernourished appearance but did not seem to be suffering. She continued to walk, but with considerable disability. The right thigh showed an enormous swelling extending from the knee to the groin. The mass was firm, not tender, and the skin glazed and pigmented; the superficial vessels were greatly dilated. The greatest circumference of the tumor measured 35 inches (88.9 cm.), and the opposite thigh measured 17 inches (42.5 cm.). The right tibia and fibula showed exostoses. The left femur and tibia also showed exostoses. The right ulna showed a marked curved deformity.

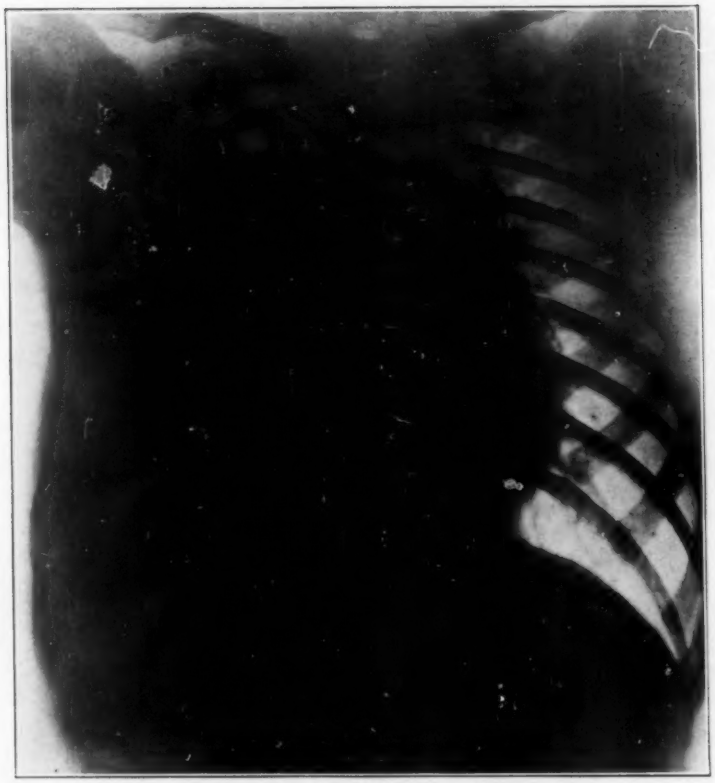

Fig. 17 (case 4).—Metastases to the lungs.

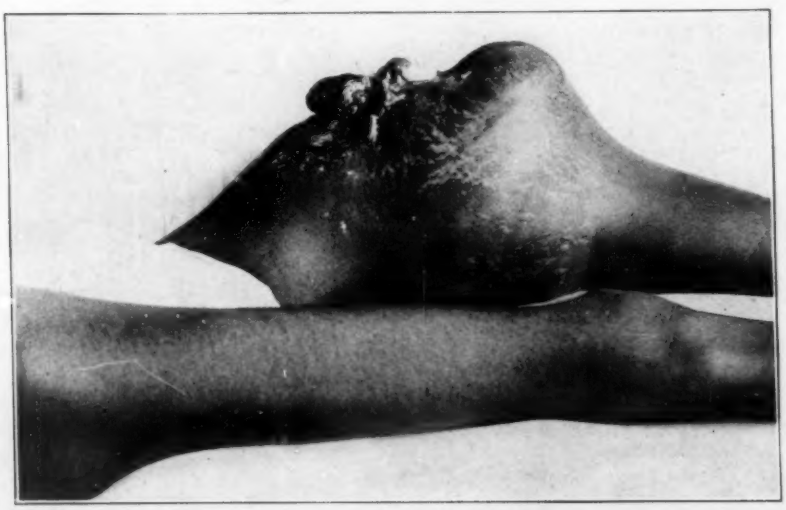

Fig. 18 (case 5).—Osteogenic sarcoma of the femur. Fungus following biopsy.

There was also a curved deformity of the left middle finger and of the left radius and ulna. The right femur is shown in figure 21. According to roentgen examination of the chest, it was doubtful whether pulmonary metastases were present.

This patient had a series of treatments with the mixed toxins of Coley combined with roentgen treatment during May, June and August, 1924. There was little if any improvement. This patient did not return for further treatment. She is dead, but I have been unable to find out the date or any circumstances of her death.

Fig. 19 (case 5).—A massive tumor, with formation of new bone, invading the soft tissues.

It is quite possible that this tumor arose as a result of injury to an exostosis of the femur.

CASE 7.—E. R., a negro, aged 35, admitted to the hospital on Nov. 24, 1914, had pain in the right heel and instep five years before admission. Later, he noticed a tumor on the outer side of the thigh just above the knee. There was little pain, and he did not see a physician for two years, when he fell and fractured the femur. He was seen at the University of Virginia Hospital at this time but refused operative treatment. Union took place, and he got along fairly

well for one year. Pain then became severe, and he had to use a cane and later was driven to the use of crutches.

He insisted on amputation at the time he entered the hospital. The lower end of the thigh was much enlarged. The tumor measured 27 cm. from the upper to the lower limit, and the greatest circumference was 64 cm. The overlying skin was normal, but the superficial veins were dilated. On palpation the mass felt like bone with cystic areas scattered throughout. At the upper limit, the tumor seemed continuous with the shaft of the femur. The patella could be palpated on the anterior and lower aspect of the tumor. Motion of the knee joint was

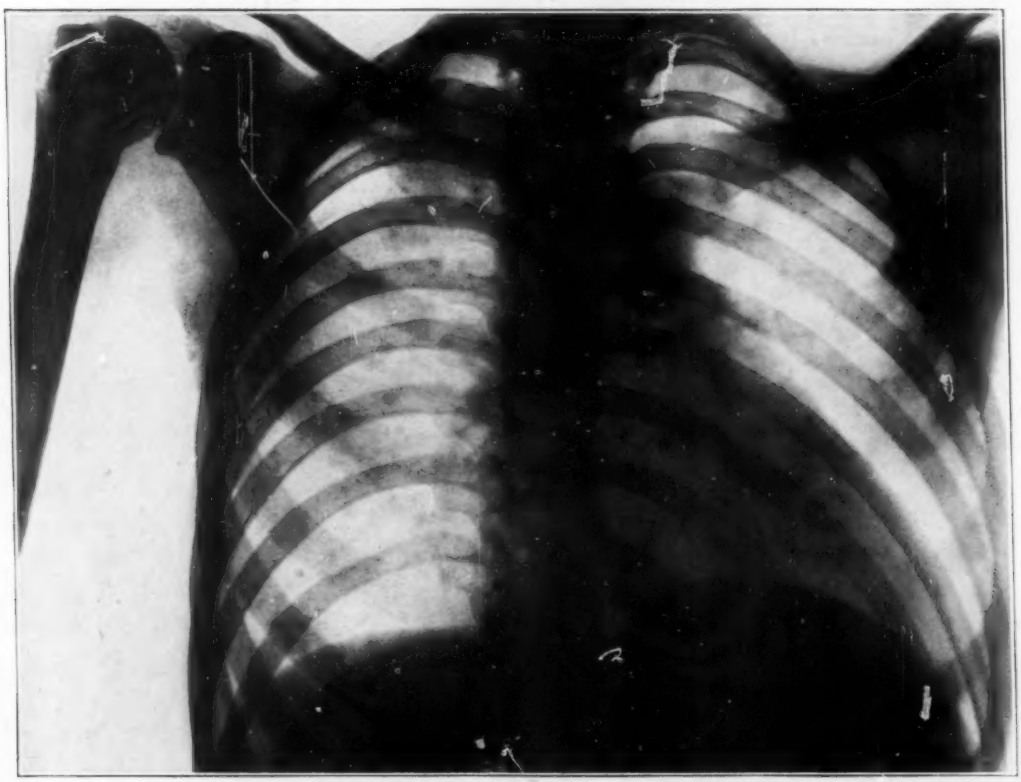

Fig. 20 (case 5).—Metastases to the lungs.

somewhat impaired and painful. The patient could not bear any weight on the extremity (fig. 22). An x-ray film of the femur (fig. 23) showed a marked cystic, loculated expansion of the cortex to a diameter of 7½ inches (19 cm.). The cortex was thin, but there was apparently no breaking through.

A diagnosis of giant cell tumor was made from the clinical and roentgen evidence.

A subtrochanteric amputation was done, with good recovery, and the patient was alive fourteen years after operation.

Case 8.—D. C., a white girl, aged 17 years, was admitted to the hospital on Aug. 18, 1925. She twisted her knee several months previously, and swelling

Fig. 21 (case 6).—Osteogenic sarcoma of the femur with marked tumor ossification and invasion.

Fig. 22 (case 7).—Giant cell tumor of the femur.

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resulted and persisted. This was aspirated by the family physician, and bloody fluid was obtained. One month before admission the patient was in an automobile wreck and fractured the upper end of the tibia. The physician advised roentgen examination, and a diagnosis of sarcoma with pathologic fracture was made. When the patient entered the University Hospital, a roentgenogram was made (fig. 24).

Fig. 23 (case 7).—Trabeculation and thin capsule, but no breaking through.

There was marked expansion of the cortex of the upper end of the tibia for a distance of about 4 inches (10 cm.). This expanded portion showed areas of rarefaction and apparent trabeculations. At certain points along the expanded cortex there was new bone proliferation running out into the soft tissues. The shaft of the tibia adjacent to the expanded portion showed what was thought to be infiltration or invasion. The shaft below the expansion showed formation

Fig. 24 (case 8).—Giant cell tumor of upper end of the tibia. Pathologic fracture.

Fig. 25 (case 8).—Sclerosis and formation of new bone after radiotherapy.

of new bone along the cortex. This was thought probably to be a giant cell tumor, although the apparent invasion into the soft tissues and into the shaft of the bone below it was against this diagnosis, and was in favor of malignant disease. After consultation, it was decided that this growth was a giant cell tumor.

A roentgen treatment was given, and the fracture was then treated with rest and fixation. Good union was obtained, and further roentgen treatments were given. The follow-up films showed a marked increase in formation of new bone throughout the entire tumor. The trabeculae were much more dense (fig. 25).

Fig. 26 (case 9).—Typical giant cell tumor of the lower end of the tibia.

CASE 9.—F. T., a negro man, aged 56, was seen in December, 1920, complaining of pain just above the left ankle of five months' duration. He attributed this pain to a trivial injury sustained six months previously. X-ray films taken at that time seemed to show a giant cell tumor of the lower end of the tibia. A Wassermann test made at that time gave a doubful reaction.

One year after the onset of the foregoing condition, the patient noticed a small mass midway between the knee and ankle of the same leg. This mass had slowly increased in size and had caused slight discomfort.

The patient was admitted to the hospital in March, 1924, and a roentgen examination was made. Figures 26 and 27 show the large area of relative rarefaction present at that time in the lower end of the tibia, just above the articular surface.

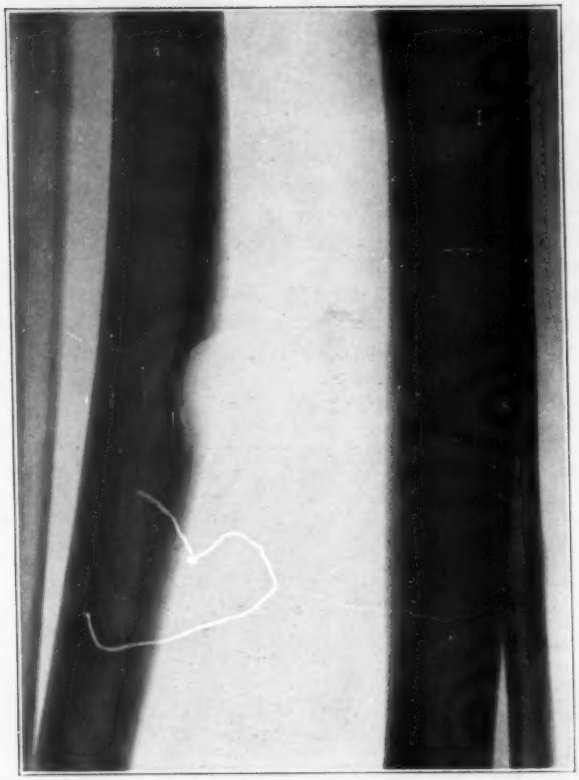

Fig. 27 (case 9).—An erosion on the shaft of the tibia.

Fig. 28 (case 9).—Increase in size of the giant cell tumor which has broken through its capsule and seems to be invading.

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This area was fairly well defined, and was apparently not invading the normal bone. There were a few small cross areas of increased density which might be striae of bone dividing this area into loculi. The area was about 2 inches (5 cm.) in length, by about 1½ inches (3.7 cm.) in diameter. Only a shell of cortex was left.

An erosion on the shaft of the tibia was also demonstrated. The patient refused treatment and was not seen again until March, 1927. He continued to have pain in this leg, but it was rarely severe enough to keep him from work. The tumor in the lower end of the tibia had increased somewhat in size, and the tumor in the shaft had increased considerably in size, measuring 16 by 10 cm.

Fig. 29 (case 9).—The site of erosion where a pathologic fracture has taken place and the tumor extending out in the soft parts and invading the marrow cavity.

Several weeks before this last admission, the patient stated that while plowing, his leg gave way under him and that he had been on crutches since. The x-ray films are shown in figures 28 and 29.

The area on the tibia which in 1924 showed a simple erosion now showed an erosion which extended entirely through the shaft. A pathologic fracture with overriding had occurred. There was apparent formation of callus between the upper and lower fragments with irregular vacuolization. There was a large soft tissue tumor over the site of the fracture. The giant cell tumor noted in the

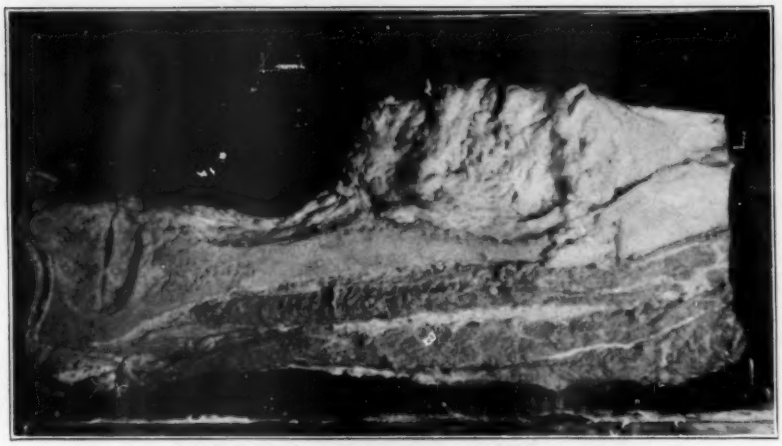

Fig. 30 (case 9).—The tumors are invading, and there is a pathologic fracture with overriding.

Fig. 31 (case 9).—Spindle and polyhedral cells.

lower end of the tibia had increased in size and was apparently breaking through the cortex. The erosive lesion of the shaft of the tibia was thought by the roentgenologist to be a gumma.

Stereoscopic films of the chest showed no pulmonary involvement. A Wassermann test made and repeated at this time was negative. A biopsy was done on the tumor of the shaft, and the report from the quick sections was that of malignant disease. An amputation at the midthigh was done (fig. 30). The tumor of the shaft was solid, gray and had areas of hemorrhage. The central portion was gelatinous. The tumor had eroded the tibia, leaving 0.5 cm. thick-

Fig. 32 (case 10).—Destruction of the shaft and neck of the femur. The tumor is partially encapsulated but breaking through and invading at one place.

ness and had extended into the narrow cavity for 3.5 cm. The lower end of the tibia presented a smaller tumor, which was firm and loculated, with dimensions of about 6 by 4 cm. It was encapsulated but firmly attached to the bone. There was extension into the marrow cavity as in the larger tumor, and this extension had a similar appearance. The tumor did not extend beyond the epiphysis.

Microscopic sections from the larger tumor (fig. 31) showed areas of loose fibrous tissue with collagen fibrils, areas of myxomatous tissue, more cellular areas, especially around the blood vessels with perithelial appearance, and a few areas of atypical hyaline cartilage. The cellular areas showed hyperchromatic

spheroidal and polyhedral cells. Another section showed solid cellular areas consisting of spindle cells which were hyperchromatic, with a number of foreign body giant cells as well as true tumor giant cells. The small tumor at the lower end of the tibia showed a cellular spindle cell type of tumor. These cells were hyperchromatic. The pathologic report was osteogenic sarcoma.

Nearly two years have elapsed since operation, and the patient is quite well.

CASE 10.—Mrs. F. G., a white woman, aged 30, was admitted to the hospital on March 16, 1927. She had been healthy until one year before admission to the hospital, when she began having severe pain in the right heel. This pain

Fig. 33 (case 10).—Gross specimen of tumor showing destruction and invasion of bone.

gradually crept upward, until the knee and then the hip became painful. Three weeks before admission, the patient had severe pain in the region of the right hip and noticed, for the first time, a mass in the region of the great trochanter. Walking became painful. This mass was diffuse, hard, not tender and firmly fixed. It measured about 12 by 10 cm. Twelve centimeters below the anterior superior spines the circumference of the right thigh was 52.5 cm. and the left thigh, 50.5 cm.

Figure 32 shows destruction of a portion of the shaft of the femur just below the trochanter, involving only the central portion at this point. The destruction

extended irregularly 3 or 4 inches (7.6 or 10 cm.) below this point. Above the lesser trochanter and extending through the neck up to the head, there was destruction of bone with marked formation of new bone. The cortex was ruptured in the region of the greater trochanter. There was a loculated formation of new bone extending for about 1½ inches (3.8 cm.) into the soft tissues lateral to the femur.

Stereoscopic films of the chest showed no definite evidence of pulmonary involvement.

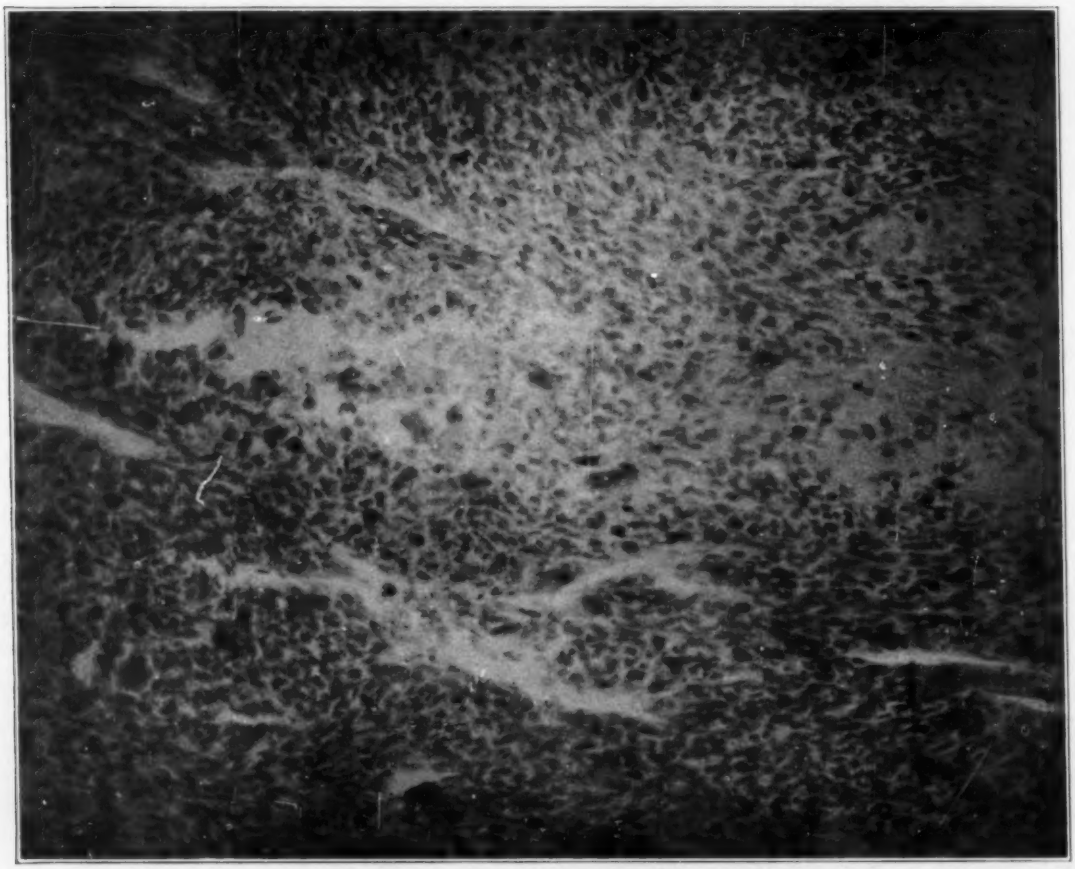

Fig. 34 (case 10).—Spindle cells and a few giant cells.

The roentgenologic report, while not conclusive, was osteogenic sarcoma, central in origin. A biopsy was done, but since a benign nature of this tumor could not be clearly established, an amputation at the hip joint was done. The gross specimen and the photomicrographic appearance are shown in figures 33 and 34.

The tumor was encapsulated, involving the greater trochanter and part of the head and neck and about 3 or 4 cm. of the shaft. Part of the tumor was red and gelatinous, but some areas were more light in color and solid. The portion in the shaft was dark red and gelatinous.

Sections from the portion in the shaft showed a vascular and fairly cellular giant cell type of tumor with areas of necrosis. Sections from the white portion near the capsule showed the same picture with large areas of necrosis and hemorrhage. The cells in this area were of the younger type and varied considerably in size and staining property, and there were fewer foreign body giant cells. There were a few spicules of old bone and an occasional true tumor giant cell. This was a cellular giant cell type of tumor, and areas showed cells which varied greatly in size and staining property, and a number of mitotic figures were present. While these tumors are benign generally, the histologic structure of this one was not entirely benign.

This patient was well almost two years after operation and was making remarkably good use of an artificial limb.

SUMMARY

My chief purpose in preparing this paper was to record in the literature and in the Registry of Bone Sarcoma some unusual cases of tumor of the bone.

Some osteogenic sarcomas are so typical in their clinical and roentgen manifestations that diagnosis is not difficult. For these patients, however, there is no satisfactory treatment, and the prognosis is poor.

The typical giant cell tumor presents such clear clinical and roentgen evidence that a diagnosis can usually be made without hesitation. The treatment for this lesion is satisfactory, and the prognosis is good.

There are variants, or borderline cases, suggesting in some respects the osteogenic sarcoma and in others the giant cell tumor. Since clinical and roentgen studies have not led to a positive diagnosis, biopsy in resorted to and even then expert pathologists will often disagree as to the benign or malignant nature of the neoplasm.

Radical operation, combined with radiotherapy and the mixed toxins of Coley, should be the treatment of choice in these borderline cases.

SKIN PRINTS

THEIR USE IN THE DIAGNOSIS OF LESIONS OF THE BREAST *

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AND
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The first definite mention of the patterns on the balls of the fingers was made in 1686 by Marcelli Malphigii, Professor of Anatomy of the University of Bologne, who spent an active life in investigating all parts of the human body by means of a recently discovered instrument, the microscope. In 1823, one hundred and thirty-seven years later, Dr. J. E. Purkinge, Professor of Anatomy of the University of Breslau, published a treatise in the form of a small octavo of fifty-eight pages. He described the wonderful arrangements and curving of the minute furrows connected with the organs of touch on the inner surfaces of the hand and foot, especially of the last phalanx of each finger, the curves, the stripes, the loops, the spirals, the whorls, etc. This was the first attempt to classify the patterns of the balls of the fingers. There was no suggestion of the application of these variations in the pattern to the problem of identification. In 1880, two Englishmen living in Asia proposed this idea through the columns of *Nature*. Like all later investigators, they employed prints instead of real fingers in their studies.

Dr. Henry Faulde of Taukiji Hospital, Tokyo, one of the observers, wrote that these prints could be used for the identification of criminals, but he did not think of the possibility of classifying the impressions or of using them for broader purposes of general identification. He discussed the various directions of study to which the new line of work might lead and anticipated practically everything that has been developed since then, such as heredity, ethnology and comparison with other mammals.

In 1890, Sir Francis Galton proved the individuality and the permanence of finger prints and devised a method of describing and

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* From the Surgical Research and Pathological Departments of Temple University School of Medicine.

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indexing any number of prints, thus rendering possible the finding of a single print or set of prints in a large collection, and by means of this putting the system on a practical basis.

The identification of persons is based on prints of the friction skin, whether it is finger prints or the larger areas of the palms or the soles and is entirely independent of the sentience or the life of the body to be identified. Disease or death, or even loss of the stratum corneum, does

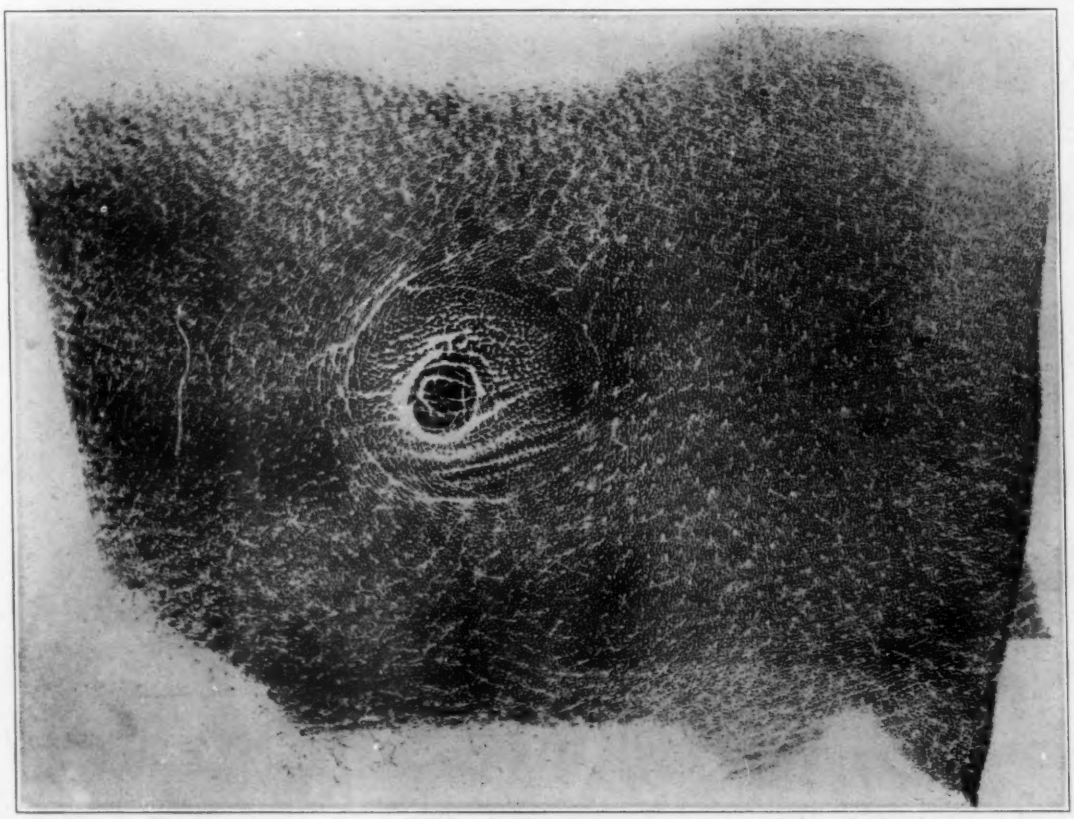

Fig. 1.—Breast of identical twin corresponding to that of twin shown in figure 2. There is no similarity noted in the size of the areola, the distribution of the pores or the corrugations of the skin.

not interfere with a proper interpretation of the skin print in the area mentioned. In the study of the epidermis covering the breast, such constancy of topography is not present. In addition to ridges, pores and the like, which are present elsewhere, there is the nipple with the orifices of the galactiferous ducts, the areola with the tubercles of Montgomery and the hair follicles.

In 1927, while examining a breast removed from an obese patient, it occurred to one of us that the changes in the skin accompanying the cancer might be depicted with printer's ink, similar to the ordinary thumb or finger print and used for teaching purposes. The pigskin appearance in this particular case was fairly marked; the microscopic observations showed a medullary carcinoma which had been noticed by the patient only six months before. The value of these prints as a diagnostic procedure soon became evident. In conjunction with the

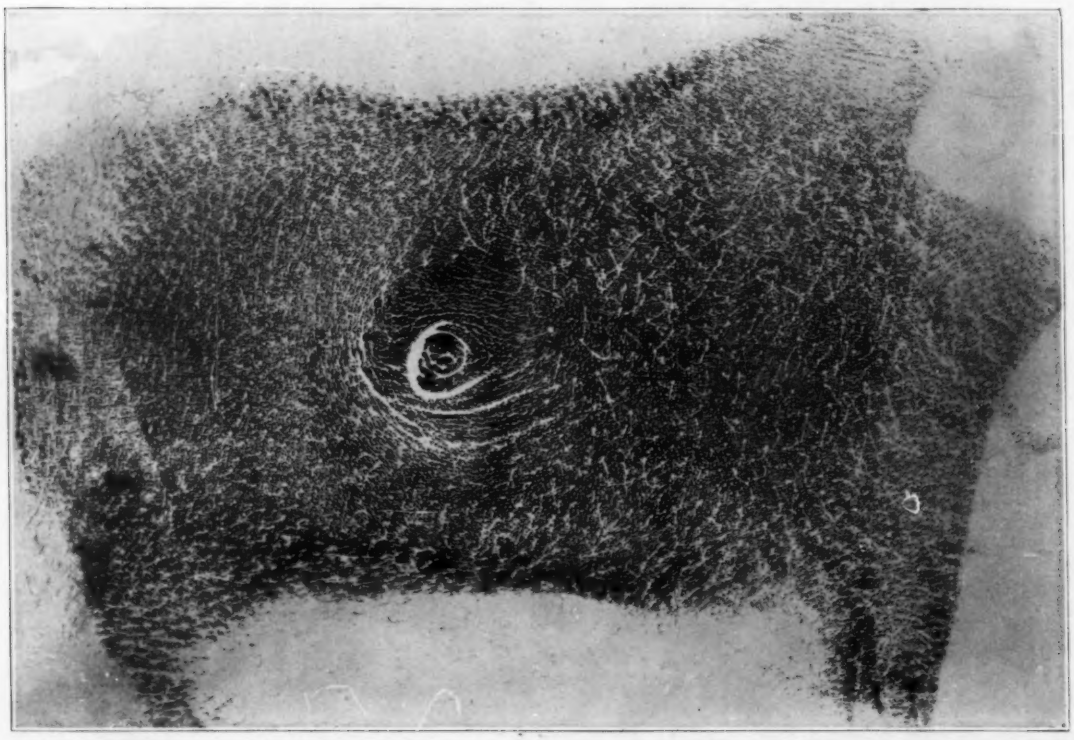

Fig. 2.—Breast of identical twin corresponding to that of twin shown in figure 1. There is no similarity noted in the size of the areola, the distribution of the pores or the corrugations of the skin.

prints, we have been making gross microscopic sections following the technic advocated by Sir G. Lenthal Cheatle of England and Dr. Wainwright of Scranton, Pa. These sections include epidermis or nipple, subcutaneous tissue, breast tissue and growth. By correlating gross and microscopic observations with the prints, we have obtained sufficient data to warrant a preliminary report. Our observations show that the pattern varies with sex and age, in the parous and nonparous

person and in the obese and emaciated person; also in the lactating and congested breast, in acute, subacute and chronic inflammation and in benign growths and cancers.

METHOD OF OBTAINING PRINTS

The following is a description of the method used. After the breast is washed with ether or alcohol, the patient is placed in the supine position with the arms on

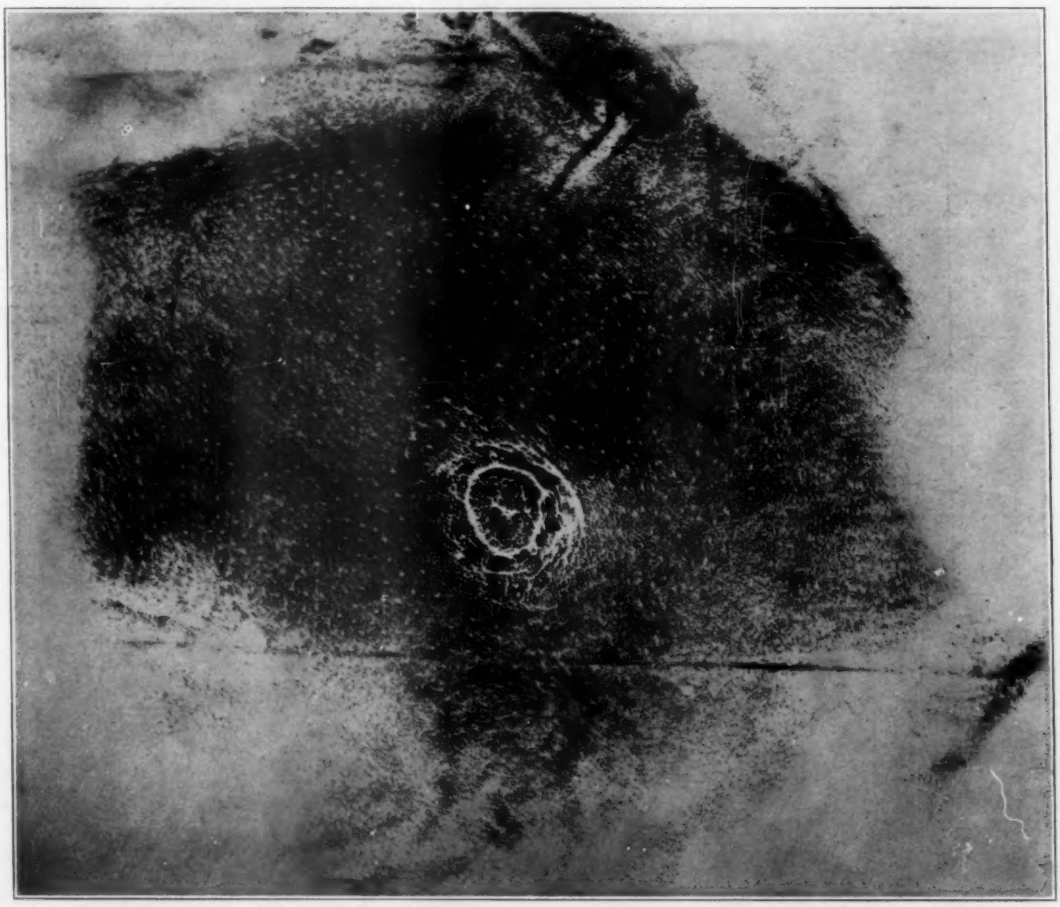

Fig. 3.—Obstructed duct; note the prominence of the tubercles of Montgomery in the affected breast as compared with the opposite lactating breast shown in figure 4.

a level with the shoulders. One should not touch the nipple with the finger, as this will usually cause it to become more prominent. The breast is anointed with ink, the outfit for taking prints of babies' feet being used. The roller should be applied vertically and horizontally to eliminate the marks made by the edges of the roller. An ordinary pad of moderately heavy white paper is selected for the print. The corners of the paper are then marked, identifying the corresponding

quadrants of the breast. A print of the normal breast should be made first. By so doing, the operator will have some idea of the degree of pressure and the amount of ink necessary. The pad is then applied to the breast from without inward with a moderate degree of pressure. It requires little practice to determine the amount of ink that should be used and the degree of pressure necessary to obtain a good print. It is best to make a series of prints; frequently, the second print is better owing to the removal of excess ink. Naturally, the posi-

Fig. 4.—Opposite breast to that shown in figure 3; the pores are smaller and more sharply defined on the affected side.

tion and the character of the lesion will at times necessitate a varying of the procedure. Sometimes the erect position may help, especially if the breast is small. At other times, the best results are obtained by attaching the paper to a cylinder, similar to a printer's roller, and rolling it over the breast. Printer's ink dries slowly. Blurring may be prevented by the spraying of "Fixatif," a volatile shellac used by artists, lightly over the print. Naturally, manipulation of the involved breast should be avoided as much as possible. Benzine, gasoline or

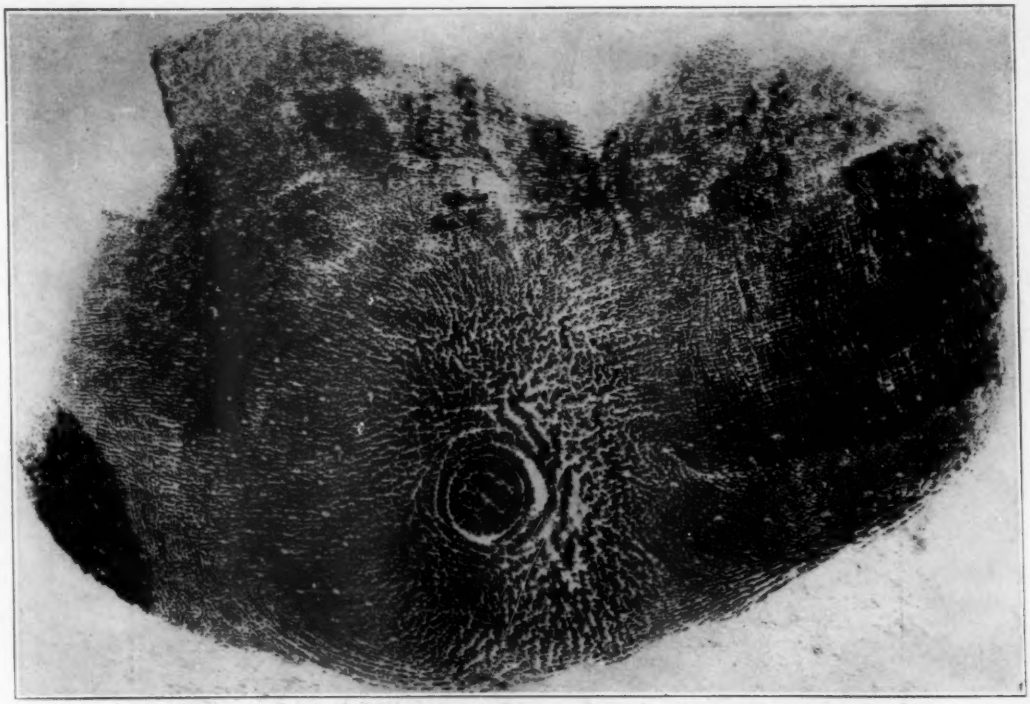

Fig. 5.—Subacute mastitis. The congestion and swelling of the breast are indicated by marked corrugations around the nipple and the wider spacing of the pores. (The very black areas were caused by adhesive plaster.)

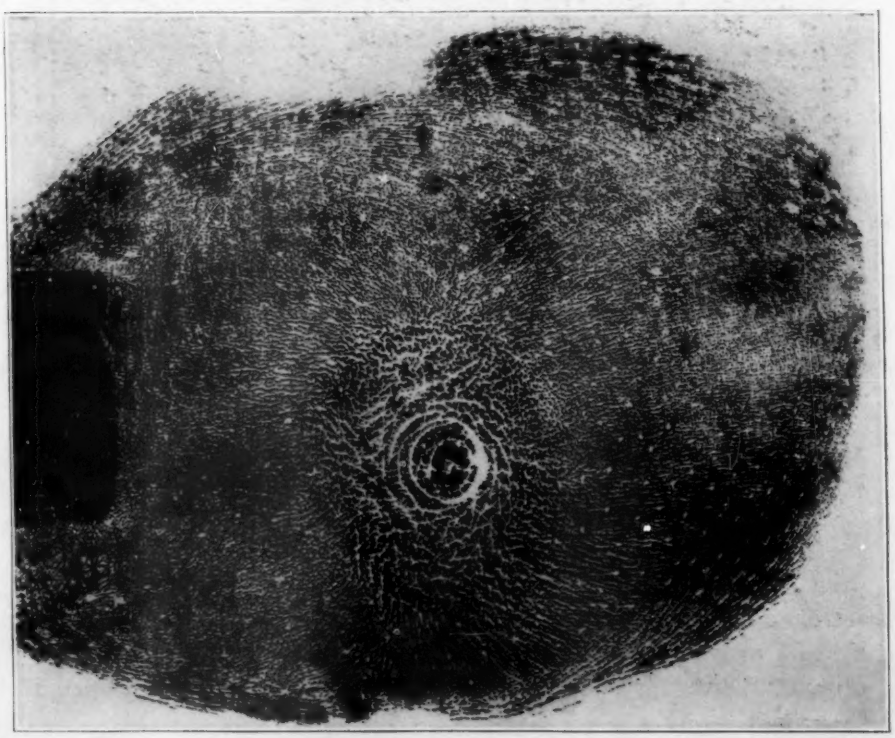

Fig. 6.—Opposite breast to one shown in figure 5.

spirits of turpentine will remove the ink. It is well to follow their use with the application of olive oil to prevent irritation.

PURPOSE OF PRINTS

We have used breast prints for the following purposes: (1) identification, (2) teaching, (3) diagnosing physiologic changes and (4) diagnosing pathologic changes.

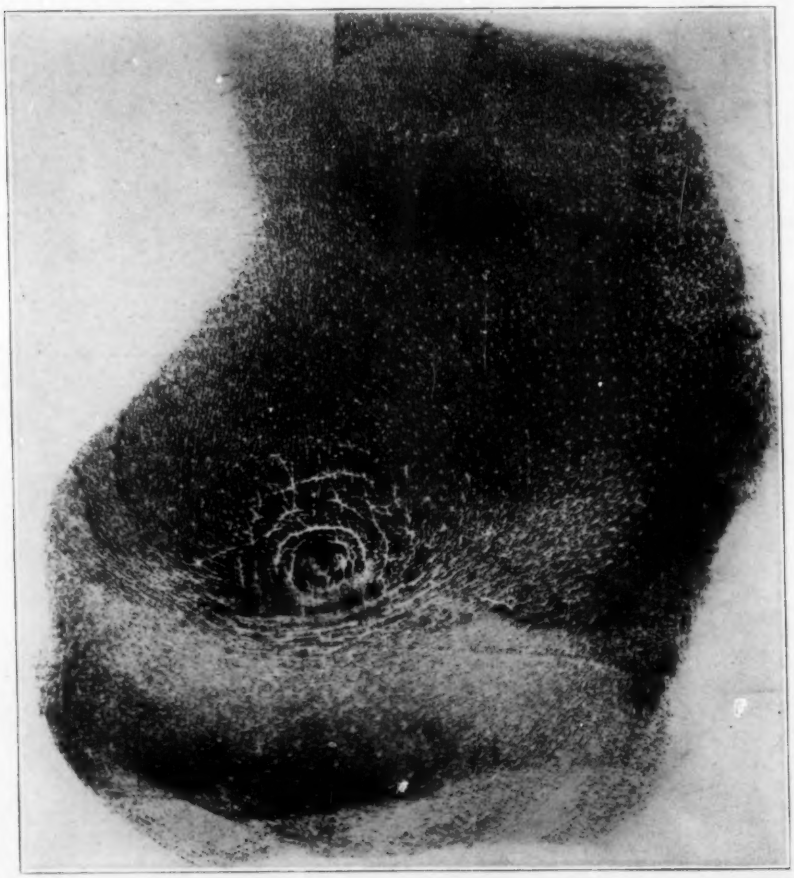

Fig. 7.—Intracanalicular fibroma. Note the even distribution, the minuteness and the wide spacing of the follicles over the tumor in the upper portion of the breast.

Identification.—Our observations seem to indicate that the breast print is as distinctive of the individual as the finger print. Figures 1 and 2 show prints of the breasts of identical twins—even without the aid of a magnifying glass a difference in topography can easily be discovered. Our study of the pores of the breast under high magnification

suggests that they are as individual in characteristics as the pores of the palm. M. Locard reported a case in which positive identification of two suspected criminals was made by means of poroscopy, prints of the palms being available only for study.

Teaching Purposes.—Skin prints portray more accurately the integument of the breast than can be demonstrated by any other method. Differentiation between physiologic and pathologic retraction of the

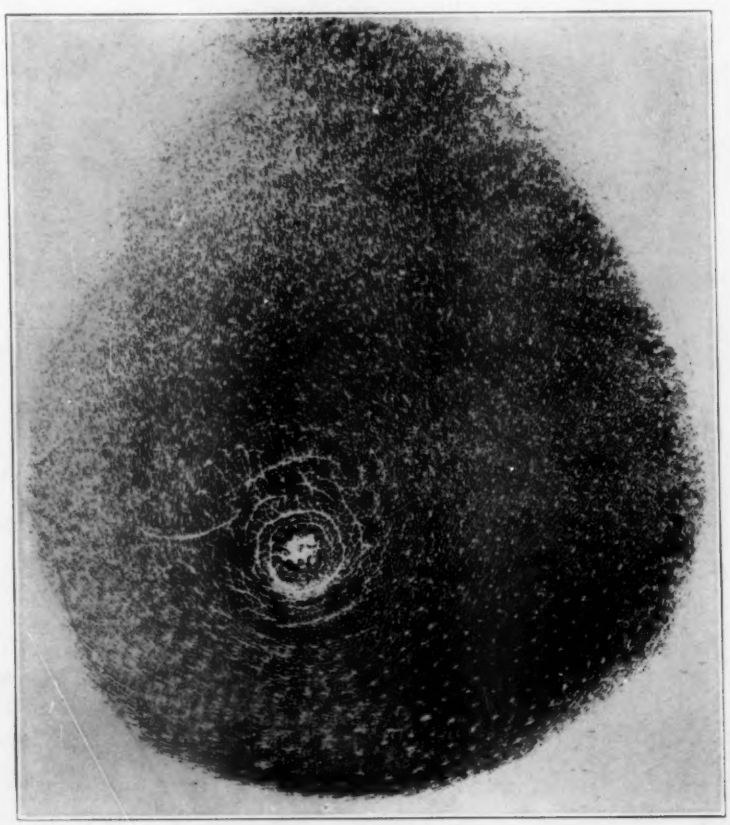

Fig. 8.—Opposite breast to one shown in figure 7.

nipple, obstruction of the ducts, accessory nipples, changes in the tubercles of Montgomery and changes in the pores can easily be noted with the naked eye. In making prints of lesions of the breast, if the growth is sufficiently dense, a definite shading outlines the size of the growth. This is not produced by increasing the pressure at this point while making the print, but is due to an increased density of the tissue beneath.

Physiologic Changes.—In prints made from the breasts of juveniles, one can observe the development of the tubercles of Montgomery, and while they make their appearance at varying ages, we have not been able to demonstrate them before the age of 4. At the present time, we are studying prints of breasts made before and during menstruation and before and during the early months of pregnancy. We are not

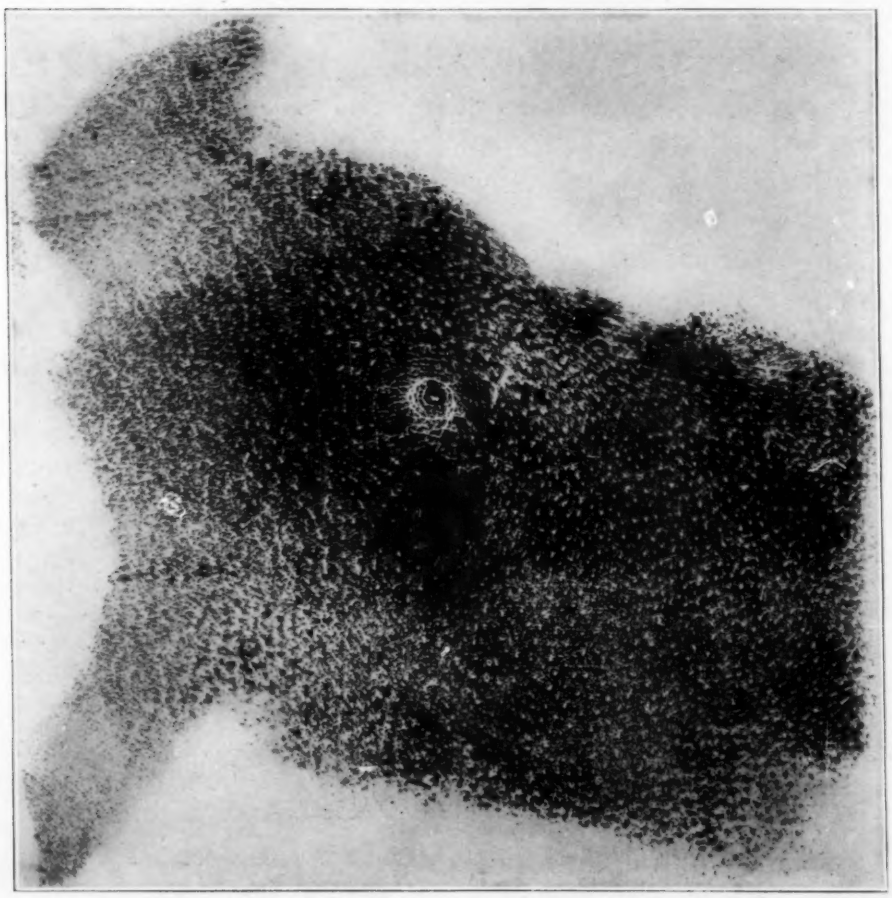

Fig. 9.—Fibro-adenoma of the breast of a man. The pores are small and are evenly spaced over the lump just beneath the nipple.

prepared to make a definite statement regarding the changes incident to the physiologic changes. Changes in the parous and nonparous women, of course, are fairly marked.

Pathologic Changes.—The pathologic changes include: (*a*) congestive, (*b*) inflammatory and (*c*) neoplastic lesions—benign or malignant.

There is apparently no change in the size of the pores in congestive lesions. In one case of obstructed duct in a parous woman, the tubercles of Montgomery were definitely accentuated.

In acute inflammatory lesions there is no marked change in the pores. In the print depicted there is a marked change in the size of the areola. The same change was observed in subacute mastitis. In Schimmelbusch's disease no change has been noted in the topography of the nipple

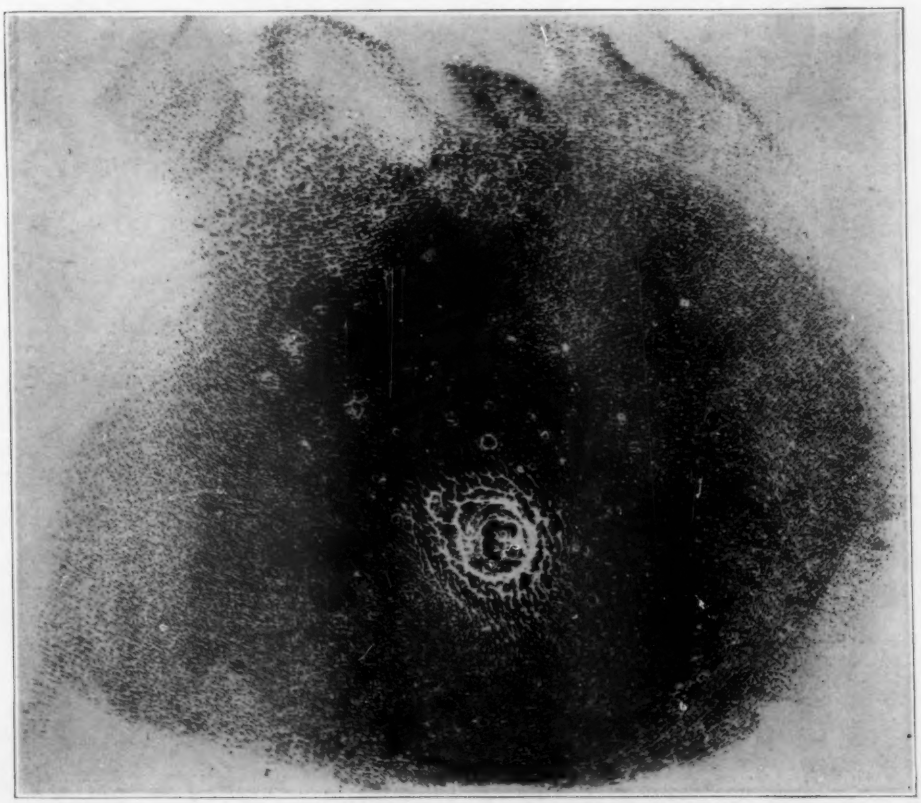

Fig. 10.—Carcinoma simplex. The irregularity and extreme minuteness of pores over the tumor should be noted. Crater-like areas of seborrheic dermatitis can be seen.

or in the size of the pores. In one print taken after operation, the pores were the same.

The topography of the integument covering benign lesions shows no gross change visible to the naked eye. So far we have been unable to note any constant change in the size and shape of the pores and no change in the tubercles of Montgomery or in the areola or nipple itself

in benign lesions. We are enlarging prints and counting and studying the shape of the individual pore. We have not advanced in the study sufficiently to draw any conclusions.

In malignant lesions, it seems possible that the changes in the integument may vary with the type of growth in the breast. We have noted the following changes: The more fibrous the growth the greater the tendency toward obliteration of the pores of the skin. In occasional persons in whom the lesion increased rapidly in size, there seemed to be

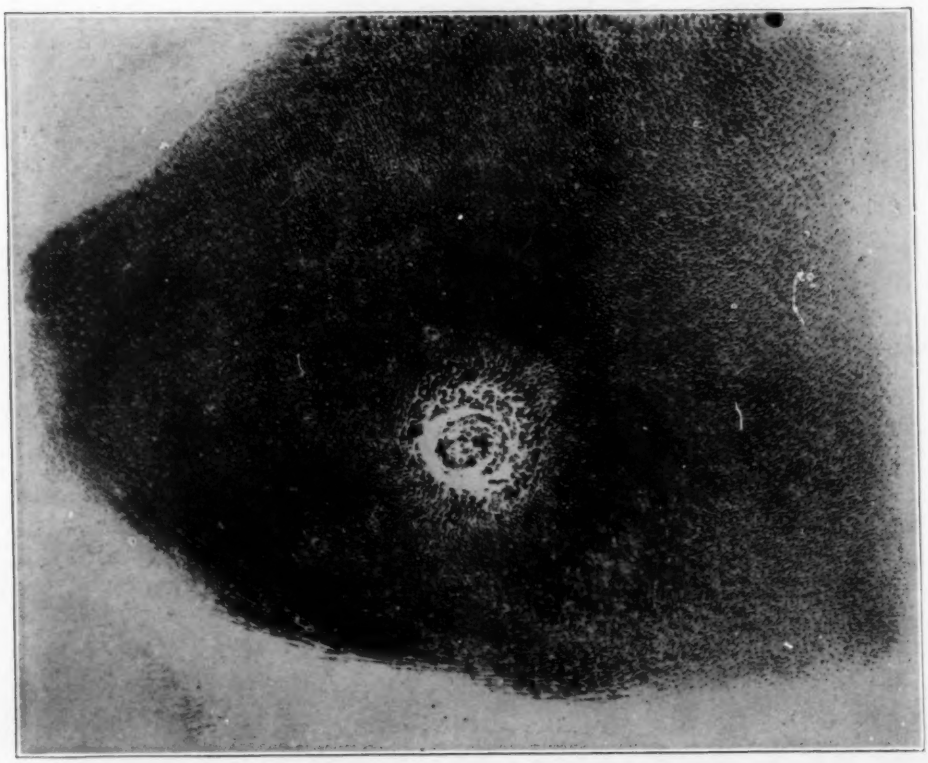

Fig. 11.—Opposite breast to one shown in figure 10.

a tendency toward marked increase in the size of the pores. We have noted this in obese women. In breasts in which carcinoma simplex has been diagnosed microscopically, the pores have been smaller. In one case, figure 10, the integument directly over the growth was covered with patches of seborrheic dermatitis. Just what relation these patches bore to the malignant growth is not known. Cross-sections of the entire breast in this case showed cancerous infiltration of the subcutaneous tissue. This was marked enough to produce a visible cupping of the epidermis over the growth. The change in topography of the nipple,

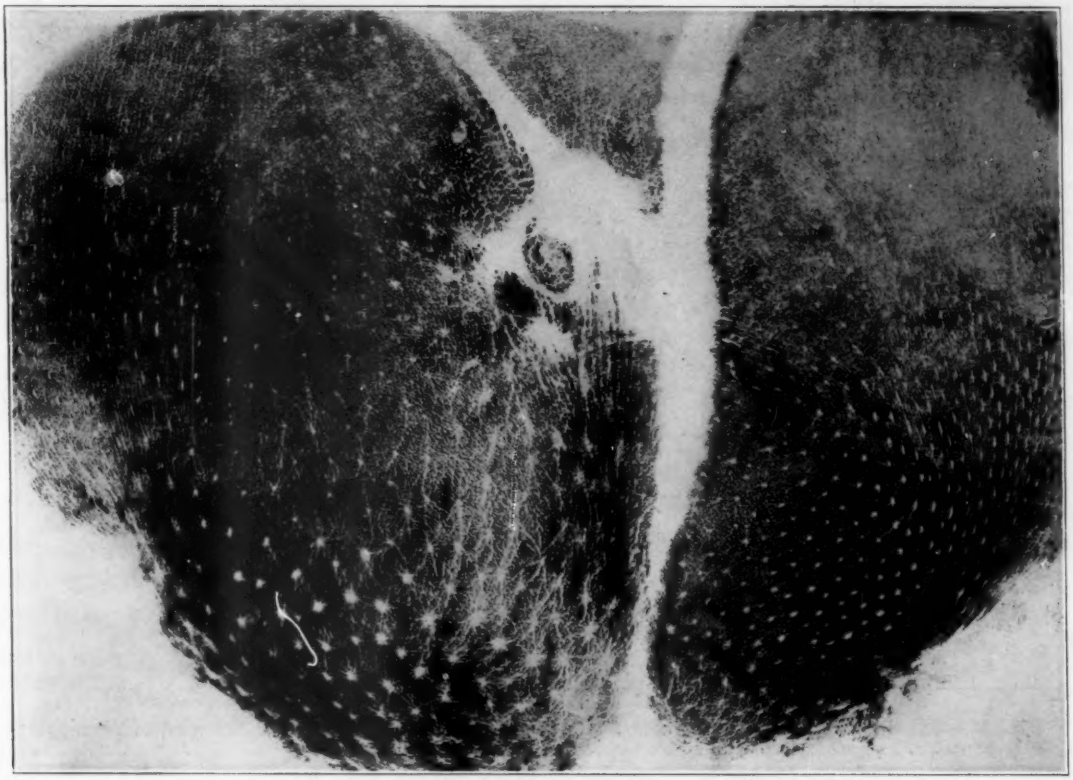

Fig. 12.—Medullary carcinoma in an obese patient (taken after removal of the breast). Extreme retraction of the nipple; large stellate pores due to edema (pigskin), and the disappearance of tubercles of Montgomery and of pores in midportion to the outer side of the nipple are shown.

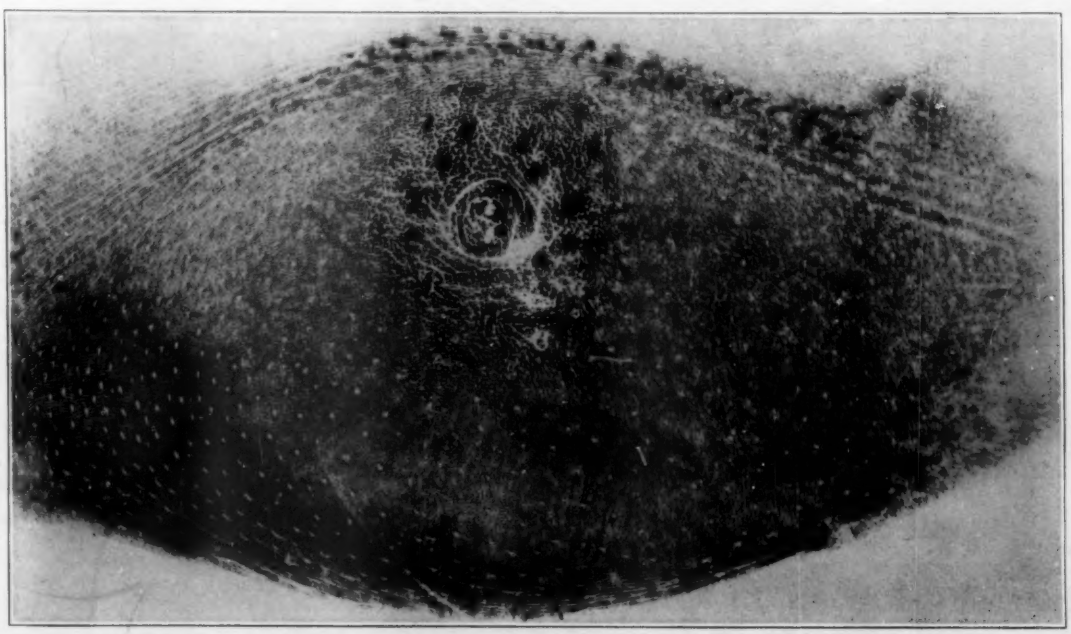

Fig. 13.—Opposite breast of the same patient in figure 12.

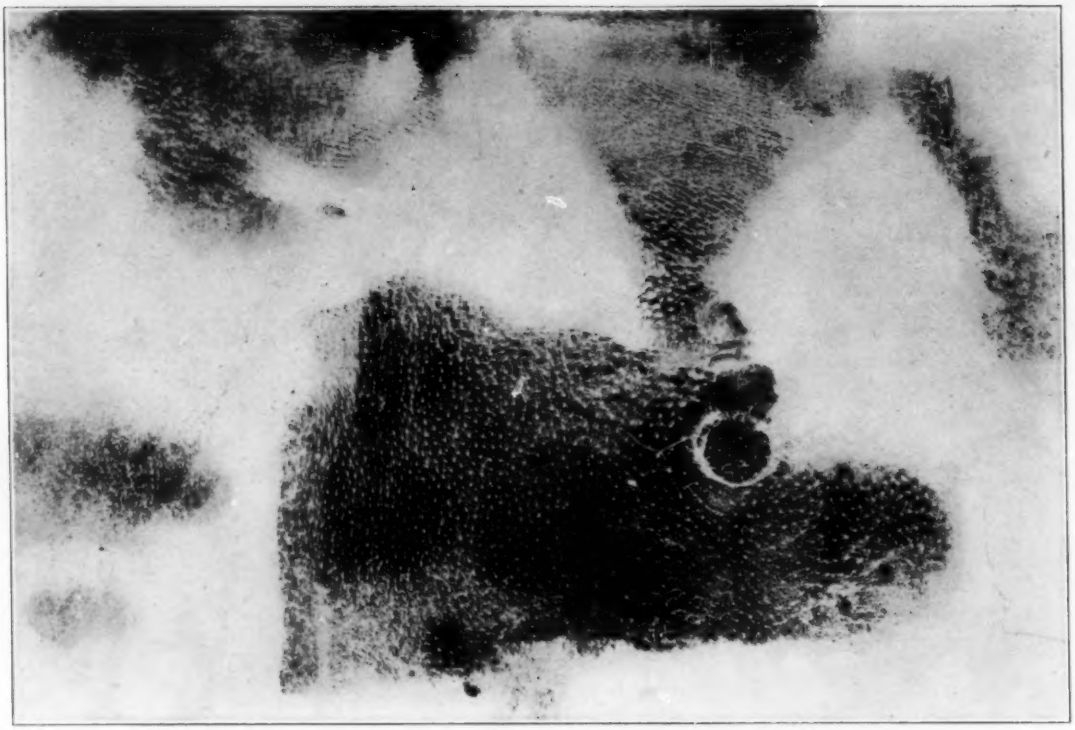

Fig. 14.—Scirrhous carcinoma; flat breast adherent to the wall of the chest. Retraction of the nipple; partial obliteration of the areola and loss of the follicles immediately surrounding it, and tendency to disappearance of the pores beyond the nipple in the upper portion should be noted.

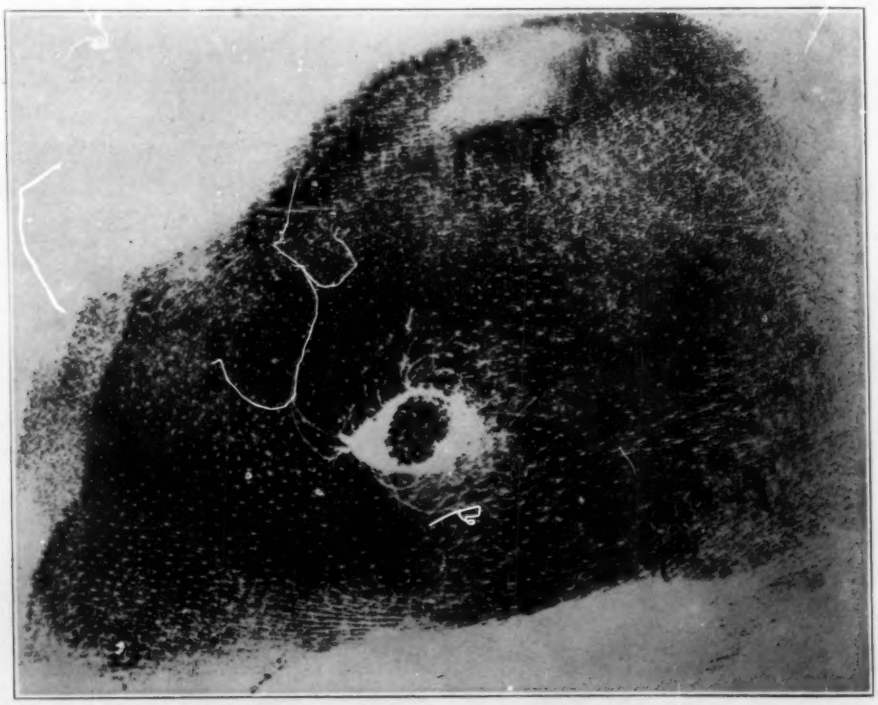

Fig. 15.—Opposite breast of the same patient in figure 14.

of course, depends on the situation of the growth; when the cancerous processes have been close enough to produce a retraction, the halo around the nipple is diminished. If the process involves the areola, there is an obliteration of the follicles.

CONCLUSIONS

1. Prints of the human breast depict certain physiologic and pathologic changes more clearly than they can be shown in any other way, making such prints invaluable for teaching purposes.

2. Lesions developing in the tissue of the breast (gland proper) produce changes in the epidermis which we believe are characteristic.

THIRTY-EIGHTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY *

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CONGENITAL DEFORMITIES

Congenital Dislocation of the Hip.—Swett [1] described a new method of operative reduction for certain long-standing congenital dislocations of the hip. The steps of the operation consisted of opening the joint capsule, freeing the upper portion of the femur from its attached muscles and of then performing an oblique osteotomy of the femoral shaft just below the trochanters. This procedure freed the upper fragment from the restraining action of the shortened soft parts, and the head could then be placed in the acetabalum quite easily. It was retained in place by overlapping and suturing the redundant portions of the joint capsule. Following the operation, the limb was fixed in plaster or treated in a Thomas splint with extension in order to maintain proper alinement of the femoral fragments. Inevitably there was a certain overriding of the fragments, but union did not fail to develop in any of the patients operated on, and the functional results were reported as satisfactory. The operation was performed on seven hips in four patients.

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* This report of progress is based on a review of 160 articles selected from 250 titles dealing with orthopedic surgery appearing in medical literature between June 9, 1928, and Oct. 15, 1928. Only those papers which seem to represent progress have been selected for note and comment.

1. Swett, Paul: J. Bone & Joint Surg. **10**:675 (Oct.) 1928.

The author claimed that this method offered a means of reduction in a type of case in which the dislocation had previously been considered irreducible. He considered that the operations thus far performed had been too few and too recent to allow of a final conclusion as to the value of the method but that the only apparent obstacle to its wider use lay in the possibility of too great a degree of disturbed or altered growth and development of the femoral head and acetabulum.

That it was possible to reconstruct the acetabulum in patients with old congenital dislocations of the hip in such a fashion as to deepen the cavity and to give the outer part of the roof a more rounded shape and thus to permit of reduction was demonstrated by Bade.[2] The technic had been worked out on the cadaver, and recently, the operation had been performed successfully on a patient, aged 27. An osteotomy was performed dividing the ilium horizontally from below the anterior superior spine, transversely through the acetabulum. The wing of the ilium carrying the upper half of the acetabulum was then sprung upward and outward from the lower portion by driving an ivory wedge into the gap. This brought the anterior spine into a lateral position in relation to the pubis and descending branch of the ichium.

Gill[3] defined his position in respect to the treatment for old or irreducible congenital dislocations of the hip. He divided the cases into three types: type 1, hips in which there was a shallow acetabulum with the head protruding beyond its upper margin but without complete dislocation; type 2, hips with complete dislocation but in which by open operation the head of the femur could be replaced in the acetabulum without great force or tension; type 3, practically all patients more than 10 years of age in whom there was upward displacement of the head of from 1 to 4 four inches and in whom the head could not be replaced in the original acetabulum at the time of operation or only by the use of excessive force.

In patients with hips of the first type, Gill did not open the capsule but turned down a flap from the ilium and acetabular margin superiorly and posteriorly and filled in the space above with bits of bone removed from the crest of the ilium. In type 2 he opened the capsule, replaced the head in the acetabulum after freeing the cavity of fibrous tissue and then formed a roof, as in type 1. In patients with hips of the third type, in which reduction was out of the question, he formed a new acetabulum by enlarging the old one and then made a roof.

He found that stability of the hip could be assured in all three types. Freedom from pain was almost constant. Mobility was always good in type 1, usually satisfactory in type 2 and quite variable in type 3.

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2. Bade, P.: München. med. Wchnschr. **75**:1711, 1928.
3. Gill, A. Bruce: J. Bone & Joint Surg. **10**:696 (Oct.) 1928.

The observations of Allison [4] led him to the conclusion that in congenital dislocation of the hip one was dealing with an embryologic defect and that one should realize that not only was the hip not normal at birth but that throughout the patient's life it would be deformed. This abnormality of growth might so deform the head of the femur as to render normal function of the hip joint impossible. It thus appeared that success or failure following any operative procedure was to some degree dependent on the foreordained changes in the upper femoral region. In other words, reduction of the dislocation did not mean a perfect hip regardless of how the reduction was accomplished. Nevertheless, reduction was necessary and should be attempted at the earliest possible time, both because at this period it was easier to accomplish and because it lessened the secondary changes induced by the faulty mechanics of the unreduced hip. Manipulative reduction in the early years might be successful and should be tried first, but force and resultant injury should be avoided. If the hip could not be reduced easily, open operation offered the better method.

[ED. NOTE.—Out of the welter of controversy that has raged over the subject of congenital dislocation of the hip during the last decade, certain conclusions are beginning to emerge. Growth deformity of the femoral head and acetabulum is the reef on which attempts at manipulative reduction in childhood are frequently wrecked. Concerning the question of how growth deformity may be lessened opinion is divided, and the opponents are ranged in hostile camps over the advantages and disadvantages of the open and the closed method. Allison's idea of an underlying embryonic defect may offer the means of a reconciliation between these opponents. The more fruitful field for investigation is now that of what to do for the old irreducible dislocation. Swett has devised a method which offers hope of diminishing the number of patients included in that category, but which is as yet untested by experience and appears to be surrounded by many pitfalls and dangers. Bade's method is chiefly of academic interest, as yet, but may be capable of development. Gill's conclusions are worthy of study, as they are based on a large experience.]

Congenital Deformity of the Astragalus.—Deutschlaender [5] reported on congenital deformity of the astragalus, stating that the condition was not rare since he had encountered it in twelve patients during the course of one year. The appearance of the foot resembled that of severe flatfoot, but differential points were readily discovered on examination. The patients complained of greater pain than was usually experienced in cases of flatfoot. The astragalus stood in nearly a vertical position,

4. Allison, Nathaniel: J. Bone & Joint Surg. **10**:687 (Oct.) 1928.

5. Deutschlaender, K.: Zentralbl. f. Chir. **55**:2848, 1928.

while the os calcis remained horizontal. The scaphoid occasionally showed abnormalities, but it was always found to occupy its normal anatomic position in the skeleton and did not contribute to the deformity of the foot. The bony prominence lying anterior to the internal malleolus was caused by the inward projection and enlargement of the head of the astragalus.

Mau, discussing Deutschlaender's paper, reported that he had obtained good results in this condition after resection of the head and neck of the astragalus.

Congenital Hallux Valgus.—Heller [6] encountered the condition of congenital bilateral hallux valgus in a child, aged 7 weeks. Basing his opinion on this case and other clinical experience and, in addition, on a review of the literature, the author stated his belief that hallux valgus might be either congenital or acquired and that a varus deformity of the first metatarsal bone might be one of the several causative factors.

Congenital Variations of the Cervical Spine.—Roger, Reboul-Lachaux and Chabert [7] made a study of variations of the cervical spine. They did not include the question of cervical ribs, pointing out that this condition manifested itself in a syndrome that was more brachial than cervical. They classified the other variations under the following headings:

Klippel-Feils' Syndrome and Occipitalization of the Atlas.

I. Klippel-Feils' Syndrome and Occipitalization of the Atlas.
   1. From the clinical point of view:
      (*a*) Shortening of the neck.
      (*b*) Low implantation of the scalp on the neck.
      (*c*) Limitation of the motions of the neck, especially in the lateral direction.
   2. From the anatomic and roentgenologic standpoint:
      (*a*) Reduction in the number of cervical vertebrae which were often atrophied and more or less fused together.
      (*b*) Ascent of the thoracic cage constituting a true cervical thorax.
      (*c*) The coexistence, among other variations, of a cervical spina bifida.

II. Occipitalization of the atlas was characterized by the following:
   1. From the anatomic and roentgenologic standpoint:
      (*a*) More or less complete fusion between the lateral masses of the atlas and the occiput, either bilaterally or unilaterally.
      (*b*) Flattening and a hazy appearance of the atlas.
      (*c*) Rotation of the atlas.
      (*d*) Frequent association of other cervical anomalies such as cervical ribs and hemivertebral axialization of the third cervical.

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6. Heller, Edward: Ann. Surg. **88**:798 (Oct.) 1928.

7. Roger, H.; Reboul-Lachaux, J., and Chabert: Paris méd. **1**:596 (June 30) 1928.

2. From the clinical standpoint:

A congenital torticollis of true bony character, especially marked in case of a unilateral fusion, but well defined even in the bilateral type. This was accompanied by a lateral inclination of the head with rotation, by a limitation of motion, especially in the lateral direction, and often by a difficulty in separating the jaws. Sometimes it was associated with a kyphoscoliosis or facial asymmetry.

The authors pointed out that although the torticollis was of congenital origin it might not manifest itself until the tenth to the twelfth years of age, the period when ossification was becoming complete.

NUTRITIONAL DISTURBANCES OF BONE

Irradiated Ergosterol in Rickets.—After a clinical experience lasting more than a year with irradiated ergosterol, Hess and Lewis [8] stated their feeling that this substance was by far the most potent of the antirachitic agents. It was an absolute specific. Cod liver oil in the amount in which it could be given was a specific of limited dependability—only moderately effective for the average infant, uncertain in action for the rapidly growing infant and ineffective for the premature infant. Treatment with irradiated ergosterol was quite as valuable in tetany as in rickets and in both disorders was remarkable for the rapidity as well as for the reliability of its action. As yet, however, sufficient clinical experience had not been acquired to define its proper dosage. Furthermore, the various preparations could not be evaluated as they had not yet been assayed on the basis of the number of curative units (rats) which they contained. The amounts now recommended and employed were unnecessarily high as shown by the fact that they induced an excess of calcium and inorganic phosphorus in the blood in the normal as well as in the rachitic infant-hypermineralization. Too great emphasis had been laid on rapidity of action. Before beginning distribution of this potent concentrate among members of the medical profession, it seemed advisable to make a more thorough clinical study of its dosage, as had been done in regard to other potent extracts. In view of its reliability, its high degree of activity and its ease of administration, irradiated ergosterol would prove a most valuable addition to the rapidly increasing fund of specific antirachitic agents.

Experimental Rickets Resulting From Lack of Sunlight.—Nonidez [9] was able to produce rickets in chicks by giving them an adequate diet but excluding all exposure to direct sunlight. Symptoms of weakness of the leg developed in the third week after this regimen had been inaugurated and went on to typical rachitic changes.

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8. Hess, Alfred, and Lewis, J. M.: Clinical Experience with Irradiated Ergosterol, J. A. M. A. **91**:783 (Sept. 15) 1928.

9. Nonidez, J. F.: Am. J. Path. **4**:463 (Sept.) 1928.

Osteomalacia.—Green-Armytage [10] reported his observations on sixty-nine patients with osteomalacia whom he had followed over a period of three years. He considered that osteomalacia was a food deficiency disease, like rickets. It exhibited multiple clinical types. Tetany and muscle paralyses were common. In some patients, the symptoms were mainly gastro-intestinal. Severe anemia was the rule. Many were so crippled that they could not stand or walk. Sometimes there was complete paralysis from the waist downward. The typical changes in the bones were not always present; they represented a late stage of the disease, and often appeared rapidly. The disease occurred in young girls at puberty and in virgins, but more commonly during lactation and during the third or fourth pregnancy. Improvement of the diet alone had no marked effect, nor did any benefit arise from the administration of calcium alone; but the addition of cod liver oil to the diet or its intravenous administration caused an immediate relief of symptoms, the hobbling, waddling, groaning cripple within a few weeks being able to walk, sit or rise from a chair without pain.

GROWTH DISTURBANCES OF THE BONE

Dyschondroplasia.—Cleveland [11] reported the case of a boy studied at the New York Orthopedic Dispensary and Hospital who was first seen in 1920, at the age of 2 years. At this time, examination showed that the left leg was 2 inches shorter than the right. Three and a half years later this leg was 6½ inches shorter, and the boy could not walk. In January, 1927, the leg was 7 inches shorter than the right. At this time, tissue was removed from the metaphysis of the tibia for study. It was found to consist of cartilage showing cystic degeneration. Except for the short leg, the patient showed a normal physical development.

The condition was chondrodysplasia of the type known as Ollier's disease and was described as an irregularity in the growth and development of cartilage localized in the epiphyses of the long bones of one side of the body with resulting skeletal deformity. Up to 1924, only fifteen cases besides this one were reported in the literature.

Larsen-Johansson's Disease of the Patella.—Larsen-Johansson's disease was described by Hawley and Griswold [12] as a condition in which there was an accessory center of ossification in the patella. It was usually bilateral and frequently associated with Osgood-Schlatter's disease of the tibial tubercle. It occurred in growing children and might give rise to indefinite pain over the patella perhaps associated with some swelling and local tenderness. The authors expressed the belief that the

10. Green-Armytage, V. B.: Indian M. Gaz. **63**:357 (July) 1928.

11. Cleveland, M.: Am. J. Surg. **5**:75 (July) 1928.

12. Hawley, George W., and Griswold, Arthur: Surg. Gynec. Obst. **47**:68 (July) 1928.

disease was essentially traumatic, resulting from a strain of the patellar ligament. Roentgen examination was necessary to establish the diagnosis.

TUMORS OF THE BONE

Osteoblastoma Simulating Osteogenic Sarcoma.—Rhoads and Blumgart [13] reported the observations in two patients with tumors of the thigh, which microscopically gave the appearance of osteogenic sarcoma. However, the tumors were unconnected with the bone. Both were removed surgically, and there had been no recurrences in the first patient in six months and in the other in two years.

From the study of these cases, the authors concluded that neoplastic bone formation might take place without any connection with primitive or adult bone forming cells. They believed that fibroblasts in any part of the body might give rise to tumor of the bone and that the bad prognosis ordinarily attached to osteogenic sarcoma did not necessarily hold true when the tumor was found unattached to bone.

Osteitis Fibrosa Cystica of the Spine.—Adson [14] made a study of two patients with osteitis fibrosa cystica of the spine and drew attention to the fact that this disease might occur in other than the long bones. Both patients were children; one presented symptoms of compression of the spinal cord, but the other complained only of pain and swelling. From his study, the author concluded that the diagnosis might be made with fair certainty from the roentgenograms but ought to be confirmed by exploratory operation, at which time as much of the tumor as possible should be removed and the remaining sac thoroughly curetted.

Hodgkin's Disease of the Bone.—The fact that Hodgkin's disease might appear primarily in bone was pointed out by Montgomery.[15] He described a case in which the vertebra, tibia and fibula were first involved and in which, only two and a half years later, the lymph nodes began to be involved. This shows the necessity of complete roentgen examination in all cases of Hodgkin's disease and the importance of examination of the osseous system in all such cases at necropsy.

BACK PAIN, SCIATIC PAIN AND OTHER PAIN

Causes of Low Back Pain.—O'Ferrall [16] believed that the majority of the acute and many of the chronic backaches occurring in young adults below the age of 45 resulted from sprain of the lumbosacral ligaments. He did not believe that abnormalities of the lumbosacral region alone could account for the symptoms of pain in the back. They were

13. Rhoads, C. P., and Blumgart, H.: Am. J. Path. **4**:363 (July) 1928.
14. Adson, A. W.: Surg. Gynec. Obst. **46**:684 (May) 1928.
15. Montgomery, A. H.: Ann. Surg. **87**:755 (May) 1928.
16. O'Ferrall, John T.: Low Back Pain, J. A. M. A. **91**:532 (Aug. 25) 1928.

a contributing cause, but the ligamentous and neurologic soft parts were the structures in which lay the real pathologic condition. The lumbosacral joint was normally unstable, and not enough emphasis had been placed on the ligamentous "guy-ropes" and the relation of the bony structures to one another, whereas undeserved importance had been given to the bony abnormalities.

Faulty posture and fatigue were considered by Ewerhardt [17] to be the chief factors in many cases of backache. In such cases pain was usually present low in the back, sometimes radiating down the thigh. Roentgen examination showed no changes or only slight changes, although anatomic abnormalities were often a contributing factor. On examination, lessened mobility of the lower spine with spasticity of the muscles was usually to be found. The fatigue posture with drooped shoulders, prominent abdomen, increased lumbar lordosis, flexed knees and pronated feet was habitual. A poorly developed postural sense was chiefly responsible, and recognition of this fact was fundamental in arriving at a successful solution of the problem.

Discussing a group of patients in which a history was obtained of a relatively sudden onset of pain in the back following a muscular movement of the "surprise type," Heald [18] suggested that the lesion was a minor tear of the inner portion of the quadratus lumborum muscle and of its anterior fascial covering, commencing at the point where it becomes continuous with the ilio-lumbar ligament. In his opinion, the injury was insufficient to cause a dislocation of a joint the size of the sacro-iliac joint. He called attention to the fact that these patients, when lying on their backs, although able to lift each leg separately with the knee extended, were unable to lift both legs together. The patients not cured by lying in bed flat with a pillow under the buttocks, followed by strapping when they were up and about again, were relieved by mobilization under anesthesia; the movement Heald considered most important was hyperextension of the thigh, with the sacrum fixed, the patient lying in the face prone position.

Referred Pain, "Sciatic" Pain.—Upson and Nielson [19] reported a series of patients demonstrating the value of roentgenography in the diagnosis of the cause of referred pain. They believed that the radicular cause of pain was far more common than was usually suspected. By tracing the skin areas of individually involved muscles to the corresponding segment of the spinal cord, the neurologist might be able to suggest the segment of the spinal cord in which the pathologic cause of the referred pain would be found. Unless it was possible to establish a definite relation between pathologic changes in the spinal column and

17. Ewerhardt, F. W.: Arch. Physical. Therapy **9**:249 (June) 1928.
18. Heald, C. B.: Lancet **2**:66 (July 14) 1928.
19. Upson, W. O., and Nielson, J. M.: Am. J. Surg. **4**:616 (June) 1928.

the site of pain, the presence of arthritis of the column should not be assumed to be the cause of the pain. Atrophy or fibrillary twitching of muscles was often a good guide to the spinal lesion; pain alone was less reliable, but objective changes in skin sensibility were of extreme importance.

Gierlich [20] stated his opinion that irritation of the root of the fifth lumbar and first sacral nerves might easily be confused with inflammation of the peripheral terminal branches of the sciatic nerve in the calf of the leg and foot unless care was employed in the examination. Severe pain on pressure at a point about 3 cm. lateral to the spinous process of the fifth lumbar vertebra was a characteristic sign of what he termed "root sciatica." In severe cases, there might develop a paresis of the peronei with typical reaction of degeneration. Weakening of the plantar reflex also denoted involvement of the root.

SCOLIOSIS

Rachitic Scoliosis.—Schede [21] expressed his conviction that the typical rachitic scoliosis resulted from the kyphosis that developed when the rachitic child was allowed to assume the sitting posture too early. The first changes noted were a diminution in the height of the eighth, ninth and tenth dorsal vertebrae, and were secondary to the development of the kyphosis. In order to make the spine erect after these changes had appeared, it was necessary for the child to make a spiral tortion above and below the hump. In many of the patients the changes did not progress, but in others the scoliosis increased with accompanying structural changes.

[Ed. Note.—The author has not produced sufficient evidence to prove his point, but his observations may be worthy of additional study.]

Vital Capacity and Muscle Study in Scoliosis.—Vital capacity was studied by Flagstad and Kollman [22] in 100 patients with scoliosis, and they reached the conclusion that there existed a definite relationship between it and the location, degree of curve and rotation of the spine. When the height of the curve was in the lower dorsal and lumbar region, vital capacity was not especially affected even in the more severe types of curvature. In mild and moderate forms of curvature, regardless of the muscle power, vital capacity was within normal limits. In severe cases, there was a difference of 13 per cent in vital capacity between the groups of patients with poor muscles and those with good muscles. This suggested that the muscles of the neck, thorax and abdomen had slight influence on vital capacity. In the opinion of the authors, study of the

20. Gierlich, N.: Med. Klin. **24**:1621 (Oct. 19) 1928.

21. Schede, F.: Ztschr. f. orthop. Chir. **49**:74, 1927.

22. Flagstad, A. E., and Kollman, Sara: J. Bone & Joint Surg. **10**:724 (Oct.) 1928.

vital capacity in such cases might give an index as to the damage done and the operative risk in thoracic, spinal and abdominal operations.

Damage of the Cord in Severe Scoliosis.—According to Jaroschy,[23] compression of the spinal cord might be encountered not only in patients with congenital scoliosis but also in those with rachitic scoliosis. The symptoms generally manifested themselves during the period of most rapid growth, from the fifteenth to the nineteenth years. The seat of the compression was generally at the level of the fourth dorsal vertebra, usually the narrowest part of the spinal canal. In the patients studied, roentgenologic examination with the aid of iodized oil showed a complete block (in one patient only a temporary block) above the summit of the main curve. In contrast to the observations in tuberculous spondylitis, radicular symptoms were completely lacking. The neurologic picture was that of a complete transverse myelitis in comparison with that of a tumor of the spinal cord in which at first the paralysis would be one sided only. The functions of the bladder and rectum were not affected. The author thought that the lesion consisted, in the early stage, of a swelling of the medulla accompanied by congestion of the blood and lymph. He believed that in the beginning it was justifiable to employ conservative and corrective treatment, but that if relief were not obtained in a short time, laminectomy should be performed. The laminae should be excised on the concave side, and the dura should not be sutured unless this could be done without tension.

Detorsion and Stabilization of the Fifth Lumbar Vertebra in Scoliosis by Operation.—Steele[24] devised an operation for scoliosis which he described as "detorsion and stabilization of the fifth lumbar." He was led to the employment of this method by his observations in a patient with scoliosis who showed a marked wedging of the fifth lumbar vertebra. Feeling that a sharp lumber curve beginning at this point was the cause of the scoliosis, he tried to correct the curve by means of plaster spicas and jackets for as long as four months or until the maximum amount of correction has been obtained. He then employed plaster jackets for about six months. It was found that there was diminution of the curve on inspection but that the only certain improvement that could be demonstrated roentgenographically was a moderate correction of the lumbar curve. This correction was gradually lost when the patient was allowed up and around without a jacket. Steele then resorted to operation to obtain correction. This was done by exposing the lateral articulations of the fifth lumbar vertebra and the sacrum and by removing their cartilage. The fifth lumbar vertebra was then lifted upward and backward by leverage and was fixed in this position by means of a specially shaped wedge of beef bone placed between the articular facets

23. Jaroschy, W.: Beitr. z. klin. Chir. **142**:597, 1928.

24. Steele, P. B.: Am. J. Surg. **4**:493 (May) 1928.

of this vertebra and the sacrum. The writer had performed this operation in six patients, but in only one had sufficient time elapsed for a final estimation of improvement to be made. This patient was followed for two years after operation, and roentgenograms showed that the change of position obtained by the insertion of the wedge between the facets had been maintained with a consequent improvement in the lumbar curve. The ordinary inspection, the symmetry of the trunk as a whole had been and still was steadily improving.

Scoliosis Treated by Fusion: Three Hundred and Forty-Eight Cases.—Risser [25] made a preliminary report of the study of end-results of 348 patients with scoliosis in whom operative fusion of the spine had been performed at the New York Orthopedic Hospital. The time period covered was from 1914 to 1926. In approximately one half of the patients, the scoliosis was due to infantile paralysis; in the remainder the etiology was undetermined, with the exception of a few in which it was due to congenital conditions, rickets and empyema.

The author concluded from this analysis that the operation of spinal fusion was one of only moderate severity. More than 50 per cent of the operations were performed in less than one and a half hours. In only a few did the postoperative temperature rise beyond 103 F. The mortality rate was 1.1 per cent. Postoperative shock and pneumonia were the causes of death. An area of natural fusion was found at operation in a few cases. In no instance was this fusion adequate to prevent an increase of deformity. Pseudo-arthrosis or failure of fusion occurred in less than 3 per cent of the cases. In these patients, there developed an increase of the curvature at the point of unsuccessful fusion.

Study of the results of the operations showed the necessity of accurate selection of the proper area for fusion. Fusion of the compensatory and not of the primary curve resulted in an increase of the deformity. In a few cases, difficulty was experienced in the determination of what constituted the primary curve. Incomplete roentgenograms were not infrequently responsible for this error. Fusion of the fifth lumbar vertebra and the sacrum was not successful, except in a few cases, in stabilizing a curvature of the lower spine. For a successful result, the stabilized area of the spine must be adequate. In not a few cases, the fusion did not extend low enough. This was especially noticed in the curvatures of paralytic origin and was most marked in those with imbalanced abdominal musculature.

In conclusion, the author stated that "spinal fusion would prevent an increase of scoliosis if the area of fusion was adequate and accurately selected; in older patients, relief from pain would be obtained. This resulted in an improvement in posture and general well being of the patient."

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25. Risser, J. C.: Am. J. Surg. **4**:496 (May) 1928.

TUBERCULOSIS

Comparing the results obtained in patients with surgical tuberculosis treated at the Edinburgh City Hospital with and without the addition of heliotherapy, Mekie [26] concluded that the results obtained by the use of artificial heliotherapy when combined with routine treatment in a sanatorium and efficient local treatment did not show any material improvement over the results obtained by treating patients by similar methods but without heliotherapy, and that therefore artificial heliotherapy has not changed the fundamental principles of the treatment for surgical tuberculosis.

Cramer [27] reported the end-results in twenty-three cases of Pott's disease in which Albee's operation had been performed from five to thirteen years previously. In only one case was a good result obtained, and in that case the acute condition healed within six months after the operation. Cramer felt that the operation is indicated only in cases which showed no tendency to spontaneous recovery on conservative treatment, and that the operation should not be done before the twelfth year.

Springer,[28] on the other hand, reported improvement in the patients' general condition following bone grafts to tuberculous spines after the method of Polya.

[ED. NOTE.—The method of Polya, usually called Henle's method in Germany, is said to be older than either the Albee or the Hibbs method. The graft is placed deeply close to the diseased vertebrae instead of being implanted in the spinous processes.]

ARTHRITIS

Small [29] isolated an organism regularly in cultures from the throats of patients suffering from rheumatic fever or chorea, and named it *Streptococcus cardio-arthritides.* Inoculated into animals, the organism produced lesions of the myocardium, pericardium and valves. Other lesions were produced in the joints, bursae, tendon sheaths and in the central nervous system. Agglutinins were found in the blood of patients suffering from chorea and acute rheumatic fever. An antiserum was obtained and its action observed in 251 cases. Prompt beneficial effects followed its use in acute chorea and in acute rheumatic fever.

Rosenau [30] discussed rheumatic fever from the epidemiologic standpoint. He regarded it as a communicable disease. He showed that

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26. Mekie, Eric C.: Brit. M. J. **2**:241 (Aug. 11) 1928.
27. Cramer: Surg. Soc. Cologne, Orthop. Clinic, Zentralbl. f. Chir. **55**:2198, 1928.
28. Springer, C.: Med. Klin. **24**:1335 (Aug. 31) 1928.
29. Small, J. C.: Ann. Int. Med. **1**:1004 (June) 1928.
30. Rosenau, M. J.: Epidemiology of Rheumatic Fever, abstr., J. A. M. A. **90**:2136 (June 30) 1928.

frank epidemics do not occur, but that there are house-to-house outbreaks. This may be due to carriers rather than to imperfect sanitation. There has been less rheumatic fever since 1918 than before. Most of the cases occurred in patients between 10 and 20 years of age, with the peak at 12. The colored race is more susceptible than the white. There is a slight predominance of females over males, except during the period of the war. It is a seasonal disease occurring in wet, cold weather. In this country it is more frequent in the spring and in England in the autumn. Like scarlet fever, acute rheumatic fever shows a downward trend as far as mortality occurs. It is related to the streptococcal family of diseases. The epidemiologic kinship confirms the impression that this is the case.

Kinnear [31] estimated that during 1927 rheumatic diseases accounted for one sixth of the total period lost from work by wage earners in Great Britain to whom sickness and disablement benefit insurance was paid. Approximately 5,000,000 pounds were disbursed under the national health insurance scheme during 1927 in Great Britain.

Swift, Derrick and Hitchcock [32] found that the general body reaction in rheumatic fever is allergic in nature probably to streptococci. The type of allergy is that found in tuberculosis and syphilis. It is not serum disease allergy but allergy due to bacterial toxin. It was found that in rabbits which had received an injection of organisms from lesions of joints of patients with rheumatic fever injection of a culture which did not have any effect on the normal rabbit would produce a lesion the size of which varied according to the sensitiveness of the so-called allergic rabbit. The animal sickened and died, showing enlarged lymph nodes and enlarged thymus. At autopsy the bone marrow showed hemorrhages similar to those following the injection of a virulent culture. The culture was really small, but the animal's reactivity had been changed. A focus is necessary to produce a state of allergy. Experiments showed that the allergic state can be removed in rabbits. The authors tried the use of vaccines without giving salicylates and obtained stormy reactions. The patient does not improve until the focus is removed.

[ED. NOTE.—The study of rheumatic fever continues to go hand in hand with the study of arthritis. We publish these abstracts to show the trend of work in that direction. The work of Swift and his associates is probably of great importance.]

Bockoven [33] reviewed 119 cases of infectious arthritis in which the patients were seen in the Veterans' Bureau Clinic. In many of these

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31. Kinnear, Walter E.: Lancet **1**:1001 (May 19) 1928.

32. Swift, H. F.; Derrick, C. L., and Hitchcock, C. H.: Allergy to Streptococcus in Its Relation to Rheumatic Fever, abstr., J. A. M. A. **90**:2137 (June 30) 1928.

33. Bockoven, S.: U. S. Vet. Bur. M. Bull. **4**:524 (June) 1928.

cases all foci had been removed, and autogenous vaccines given with no improvement in the arthritis, the disease often progressing in spite of the treatment. According to the author, undiscovered secondary foci may explain this situation.

Gordon [34] reported two cases of chronic articular rheumatism of the spine in which there were symptoms of progressive degeneration of the spinal cord. In both cases, the motor tract only was involved. There was not spasticity, but weakness with increased reflexes; no atrophy was present. The duration in these two cases was from seven to ten years. This condition may easily be overlooked in the early phases of its development. In all cases of oncoming weakness or paresis of the limbs, with or without atrophy, when no cause can be found readily, roentgenograms of the spine should be taken. The author discussed the differential diagnosis between this condition and spastic paraplegia and multiple sclerosis. He expressed the belief that the condition is due to the passage of motor and sensory nerve fibers through an intervertebral foramen which is either narrowed or inflamed by the chronic rheumatism. This condition, he stated, is infrequent.

[ED. NOTE.—While the condition here noted has been previously described, its frequency is probably greater than we are accustomed to believe.]

PYOGENIC DISEASES

The experiences of others with the Orr method in osteomyelitis have not been frequently seen in the literature. Brickner [35] did not agree with Orr in several points—not only in the entire avoidance of antiseptics but in the long delay before the first dressing and in the complete immobilization of the part in plaster.

In a series of twenty-four experiments on rabbits, Shands [36] made injections of *Staphylococcus aureas* into the knee joints and studied the effect of sterilizing the joints with gentian violet. A 4 per cent solution of the dye in dextrose was more effective than a solution with sterile water or olive oil, and 85 per cent of the animals were effectively sterilized.

POLIOMYELITIS

Flexner [37] reviewed the great epidemiologic events of the past quarter of a century. An account of the pandemics of epidemic cerebrospinal meningitis, poliomyelitis and epidemic or lethargic encephalitis is given. He believed that in earlier times these were all included in a single chain

34. Gordon, A.: Ann. Int. Med. **1**:819 (April) 1928.

35. Brickner, W. M.: Am. J. Surg. **4**:476 (May) 1928

36. Shands, A. R., Jr.: Pyogenic Arthritis in Knee Joints of Rabbits, Arch. Surg. **16**:1039 (May) 1928.

37. Flexner, Simon: Obvious and Obscure Infections of Central Nervous System, J. A. M. A. **91**:24 (July 7) 1928.

of causation and probably occurred in connection with the periodic outbreaks of influenza. Modern strides have isolated these various diseases, and in some cases have given methods of prevention and even of cure.

Aycock and Luther [38] reported their experiences with convalescent serum in 106 cases of poliomyelitis in which the patients were seen in the preparalytic stage. By a numerical method of estimation, the average degree of paralysis in the patients receiving treatment was 19 compared to an average of 63.6 in 482 patients not receiving treatment. Furthermore, the amount and severity of the paralysis varied with the interval elapsing between the onset of the disease and the time of treatment, those patients treated on the first day of the disease developing much less paralysis than those treated on subsequent days. The authors concluded, therefore, that there is a favorable effect of convalescent serum when administered in the preparalytic state of poliomyelitis as shown by (1) the low mortality rate, (2) a low average rate for total paralysis, and (3) a strikingly low rate for paralysis of the severer grades.

The intramuscular use of convalescent serum in poliomyelitis was reported by Shaw and Thelander.[39] In a series of eighty-one patients, forty-three of whom received convalescent serum intramuscularly during the active stage of the disease, only thirteen showed paralysis, while of thirty-eight not treated thirty-three showed residual paralysis.

[Ed. Note.—These reports tend to place the treatment with convalescent serum on a fairly sound basis. The early diagnosis (preparalytic) is absolutely necessary, however, to make this treatment effective.]

Flexner and Stewart [40] pointed out that the use of convalescent serum is based on experimental work done on monkeys. Because of this, they suggested that in the event of severe epidemics passive protection may be afforded to persons menaced by the disease by means of such convalescent serum.

In the last decade three types of serums have been used in poliomyelitis—convalescent serum, Rosenow's antistreptococcus serum and Pettit's serum. Stewart and Haselbauer [41] studied the neutralizing action of both Pettit's and Rosenow's serums on the virus of poliomyelitis. Monkeys were used. The poliomyelitis virus was the Rockefeller Institute strain and was obtained from Dr. Aycock. The Rosenow serum

38. Aycock, Lloyd, and Luther, Eliot: Preparylitic Poliomyelitis, J. A. M. A. **91**:387 (Aug. 11) 1928.

39. Shaw, E. B., and Thelander, H. E.: Intramuscular Use of Convalescent Serum in Treatment of Poliomyelitis, J. A. M. A. **90**:1923 (June 16) 1928.

40. Flexner, Simon, and Stewart, Fred: Protective Action of Convalescent Poliomyelitis Serum, J. A. M. A. **91**:383 (Aug. 11) 1928.

41. Stewart, F. W., and Haselbauer, P.: J. Exper. Med. **48**:431 (Sept. 1) 1928.

was obtained from Eli Lilly & Co. Dr. Pettit furnished his antipoliomyelitis serum. For controls, convalescent human, convalescent monkey, normal monkey, normal horse and normal sheep serums were used. After the serums and virus had been given ample time for neutralization in vitro, they were used in intracerebral inoculations of monkeys.

The authors concluded that Rosenow's antistreptococcus serum, concentrated or unconcentrated, does not neutralize poliomyelitis virus as tested in monkeys. Pettit's antipoliomyelitis horse serum neutralizes the virus of poliomyelitis only occasionally. Immune sheep serum, prepared according to the method of Pettit, did not neutralize poliomyelitis virus even when the normal serum of the same animals neutralized the virus. The reason for such chance neutralization of virus by normal serum is obscure and must not be confused with the constant virus-neutralizing action of both monkey and human convalescent serums. There is no experimental evidence as a basis for using either Rosenow's or Pettit's serum.

A number of observers have isolated streptococci from tissues of human beings with poliomyelitis and claim for these streptococci partial or complete fulfilment of Koch's postulates. Long, Olitsky and Stewart [42] made a study of streptococci isolated from monkeys affected with experimental poliomyelitis and of three strains of streptococci obtained from Dr. Rosenow. These workers found that a variety of ordinary bacteria, including nonhemolytic streptococci, can be recovered from cultures of the brain of monkeys affected with poliomyelitis. The bacteria were similar to those often recovered from the air of the place in which the cultures were made. The authors could find no etiologic relationship between any of these streptococci and poliomyelitis. Intracerebral injections did not produce poliomyelitis, but purulent meningoencephalitis.

[ED. NOTE.—These experimental observations further strengthen the argument for the use of convalescent serum as opposed to the use of the various streptococcic serums.]

Dickson [43] reported some satisfactory results in stabilizing hips in which the gluteus maximus and gluteus medius are paralyzed. He detached the tensor fasciae femoris from its attachment near the anterior superior spine of the ilium, and transplanted it to a point near the posterior superior spine.

Persons with paralysis of the deltoid were treated by Riedel [44] by transplantation of muscle from three directions. He dislikes arthrodesis

42. Long, P. H.; Olitsky, P. K., and Stewart, F. W.: J. Exper. Med. **48**:431 (Sept. 1) 1928.

43. Dickson, Frank: J. Bone & Joint Surg. **10**:712 (Oct.) 1928.

44. Riedel, G.: Ergebn. d. Chir. u. Orthop. **21**:489, 1928.

because of the winglike scapula produced. For anterior paralysis he uses the pectoralis muscle, for paralysis of the medial portion, the trapezius muscle, and for paralysis of the posterior portion transplantation of both ends of the teres major is recommended.

Jeletzki [45] substituted silk ligaments from the knee flexor muscles for paralysis of the calf group in three cases. The results are said to be satisfactory.

[Ed. Note.—Silk ligaments are not a satisfactory method of handling deformities and paralyses caused by poliomyelitis. We thought that they were entirely obsolete.]

VASCULAR DISEASES

After a comprehensive review of the literature and a large clinical experience, Painter [46] said that as the literature stands today it seems to him that the two significant etiologic factors are, first, a highly sensitized nervous system and vasomotor nerves peculiarly responsive to stimuli from the circulating blood; second, toxic irritants in the form of chemical alkaloids, such as nicotine, which find opportunity, because of retardation of flow and by roughening of the intima, to provide a matrix for the formation of a white thrombus. Because nature puts forth two efforts toward cure, namely, canalization and the development of collateral circulation, Painter advocated prolonged rest and the omission of tobacco as the most reasonable method of treatment.

In a study of the effect on the temperature of ligation of the politeal vein in thrombo-angiitis obliterans, Morton and Pearse [47] found an increase in surface heat. In all but two cases, there was a coincident clinical improvement in the limb. Their possible explanations are: 1. Manipulation of the vein may result in derangement of the vasomotor mechanism. 2. Possibly occlusion of the deep vein shunts the blood through the superficial vessels, thus causing an increase in temperature of the skin.

DISEASES OF THE NERVOUS SYSTEM

McFadden [48] considered most cases of obstetric paralysis due to injury of the suprascapular nerves and expressed the belief that rotation of the head combined with traction downward on the shoulder is the most common factor in causing the injury.

[Ed. Note.—Such a view can only be condemned as obsolete. The anatomic changes in obstetric paralysis have been so clearly shown by Sever, A. S. Taylor, and others that there seems little need for any attempt at a new explanation of the condition.]

(To be continued)

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45. Jeletzki, A.: Abstr., Zentralbl. f. Chir. **55**:2998, 1928.
46. Painter, Charles F.: New England J. Med. **199**:598 (Sept. 27) 1928.
47. Morton, John, and Pearse, Herman: Ann. Surg. **88**:233 (Aug.) 1928
48. McFadden, George: J. Bone & Joint Surg. **10**:661 (Oct.) 1928.

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